STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 128275

TO: Rebecca Cook **Location: REM/4C70** **Art Unit: 1614** **Wednesday, August 04, 2004** **Case Serial Number: 09/243030**	**From: Barb O'Bryen** **Location: Biotech-Chem Library** **Remsen 1A69** **Phone: 571-272-2518** **barbara.obryen@uspto.gov**

Search Notes

Dan Brazen

1282975

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

Requestor's Name: Rebecca Cook Serial Number: 09/243030

Date: 7/27/04 Phone: Rem 4C70 Art Unit: 1614

Search Topic: Inv Michael Gerard Tovey

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).

(1) Please search on cellulose ether that virus of claims 25-27

See list in claims 3: -15

(2) What are known routes of administration & dosage amounts

Thanks

Rebecca

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STAFF USE ONLY

Date completed: 8-4-04

Searcher: Doris

Terminal time: 78

Elapsed time: prep 25

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

_____ Structure

25 Bibliographic

Vendors

_____ IG

348 STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (9-90)

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=> fil medl
FILE 'MEDLINE' ENTERED AT 10:53:48 ON 04 AUG 2004

 FILE LAST UPDATED: 3 AUG 2004 (20040803/UP). FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d iall l18 4 36 34 32 14; d iall l19 17 11 10 9 7 6 3; d iall l15 13 12 10 7 6 3

L18  ANSWER 4 OF 38     MEDLINE on STN
ACCESSION NUMBER:    2004105204     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 14996694
TITLE:               Summaries for patients. Duration and dose of antiviral
                     treatment for chronic hepatitis C.
COMMENT:             Comment on: Ann Intern Med. 2004 Mar 2;140(5):346-55.
                     PubMed ID: 14996676
AUTHOR:              Anonymous
SOURCE:              Annals of internal medicine, (2004 Mar 2) 140 (5) I67.
                     Journal code: 0372351. ISSN: 1539-3704.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Commentary
                     Journal; Article; (JOURNAL ARTICLE)
                     (PATIENT EDUCATION HANDOUT)
LANGUAGE:            English
FILE SEGMENT:        Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH:         200403
ENTRY DATE:          Entered STN: 20040304
                     Last Updated on STN: 20040312
                     Entered Medline: 20040311
CONTROLLED TERM:     Check Tags: Female; Human; Male
                      Adult
                     *Antiviral Agents: AD, administration & dosage
                      Antiviral Agents: AE, adverse effects
                      Double-Blind Method
                      Drug Administration Schedule
                      Drug Therapy, Combination
                      Genotype
                      Hepacivirus: GE, genetics
                     *Hepatitis C, Chronic: DT, drug therapy
                      Hepatitis C, Chronic: VI, virology
                       *Interferon Alfa-2a: AD, administration & dosage
                      Interferon Alfa-2a: AE, adverse effects
                       *Polyethylene Glycols: AD, administration & dosage
                        Polyethylene Glycols: AE, adverse effects
                     *Ribavirin: AD, administration & dosage
                      Ribavirin: AE, adverse effects
CAS REGISTRY NO.:    36791-04-5 (Ribavirin); 76543-88-9 (Interferon Alfa-2a)
CHEMICAL NAME:       0 (Antiviral Agents); 0 (Polyethylene Glycols); 0
                     (polyethylene glycol-interferon alfa-2A)

L18  ANSWER 36 OF 38     MEDLINE on STN
ACCESSION NUMBER:    90203713     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 2156945
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Note: Interferon Alfa = recombinant Interferon Alpha

TITLE: Randomized, double-blind, placebo-controlled, patient-initiated study of topical high- and low-dose interferon-alpha with nonoxynol-9 in the treatment of recurrent genital herpes.

AUTHOR: Sacks S L; Varner T L; Davies K S; Rekart M L; Stiver H G; DeLong E R; Sellers P W

CORPORATE SOURCE: Department of Medicine, University of British Columbia Herpes Clinic, University Hospital-UBC Site, British Columbia Centre for Disease Control, Vancouver.

SOURCE: Journal of infectious diseases, (1990 Apr) 161 (4) 692-8. Journal code: 0413675. ISSN: 0022-1899.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199004

ENTRY DATE: Entered STN: 19900601
Last Updated on STN: 19970203
Entered Medline: 19900427

ABSTRACT:
To explore further topical antiviral therapy for recurrent genital herpes, 188 culture-proven patients were randomized to receive treatment with topical interferon-alpha in high-dose (10(6) IU/g with 1% nonoxynol-9 in 3.5% methylcellulose) or low-dose (10(3) IU/g with 0.1% nonoxynol-9 in 3.5% methylcellulose) treatments or placebo (3.5% methylcellulose, alone), applied three times daily for 5 days. Of these, 105 experienced prodromal symptoms within the study period and applied the medication, of whom 99 could be evaluated for efficacy. Patients were followed with daily clinical assessments and cultures until reepithelialization. The median time to negative virus culture in high-dose recipients was 2.5 days compared with 3.9 days for placebo recipients (P = .023), and a significant dose response was observed (P = .016). Antiviral effects were more prominent in men than women. High-dose recipients also had reduced median duration of symptoms to 2.7 days from 3.7 days for placebo recipients (P = .03), with a significant dose-response relationship (P = .047). Effects on duration of symptoms were more prominent in women. Times to complete reepithelialization in those who applied the drug during the prodromal phase were 5.8 days for high-dose recipients compared with 6.5 days for placebo recipients (P = .053). A multivariate ranked linear model analysis of four efficacy variables (crusting, healing, virus shedding, symptom duration) also favored the high-dose gel (P = .015). High-dose topical interferon-alpha preparation is effective for patients with recurrent genital herpes. Applied early in the course of a recurrent episode, this treatment is safe and may provide a topical alternative to other types of therapy in the future.

CONTROLLED TERM: Check Tags: Female; Human; Male; Support, Non-U.S. Gov't
Administration, Topical
Adult
Dose-Response Relationship, Drug
Double-Blind Method
*Herpes Genitalis: TH, therapy
***Interferon Type I: AD, administration & dosage**
Interferon Type I: TU, therapeutic use
Middle Aged
Nonoxynol
***Polyethylene Glycols: AD, administration & dosage**
Randomized Controlled Trials
Recurrence
Sex Factors

CAS REGISTRY NO.: 26027-38-3 (Nonoxynol)

CHEMICAL NAME: 0 (Interferon Type I); 0 (Polyethylene Glycols)

L18 ANSWER 34 OF 38 MEDLINE on STN
ACCESSION NUMBER: 96028195 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7473553
TITLE: N-acylated alpha-amino acids as novel oral delivery agents for proteins.
AUTHOR: Leone-Bay A; Santiago N; Achan D; Chaudhary K; DeMorin F; Falzarano L; Haas S; Kalbag S; Kaplan D; Leipold H; +
CORPORATE SOURCE: Emisphere Technologies, Inc., Hawthorne, New York 10532, USA.
SOURCE: Journal of medicinal chemistry, (1995 Oct 13) 38 (21) 4263-9.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19990129
Entered Medline: 19951128

ABSTRACT:
A series of N-acylated alpha-amino acids were synthesized and shown to improve the oral delivery of two protein drugs, salmon calcitonin (sCT) and interferon-alpha. Forty-five compounds in this series were tested in vivo in rats and primates. A significant positive correlation was found between the log P of the acylated amino acids and the decrease in serum calcium following oral dosage of sCT in rats. Such a correlation was not found for interferon-alpha. These derivatized amino acids only weakly inhibited the activity of trypsin or leucine aminopeptidase. Histological examinations of rat intestinal tissue after oral dosing of acylated amino acid/protein combinations revealed no detectable pathology.

CONTROLLED TERM: Check Tags: Male
Acylation
*Amino Acids: CH, chemistry
Animals
*Calcitonin: AD, administration & dosage
Calcium: BL, blood
***Drug Carriers**
Enzyme Inhibitors
Glycine: AE, adverse effects
*Glycine: AA, analogs & derivatives
Glycine: CS, chemical synthesis
Glycine: PD, pharmacology
***Interferon-alpha: AD, administration & dosage**
Intestines: AH, anatomy & histology
Intestines: DE, drug effects
Kinetics
Leucine: AE, adverse effects
*Leucine: AA, analogs & derivatives
Leucine: CS, chemical synthesis
Leucine: PD, pharmacology
Leucyl Aminopeptidase: AI, antagonists & inhibitors
Macaca mulatta
Rats
Rats, Sprague-Dawley
Structure-Activity Relationship
Trypsin: ME, metabolism
Trypsin Inhibitors

CAS REGISTRY NO.: 121428-84-0 (N-cyclohexanoylleucine); 28172-57-8 (N-cyclohexanoyl-2-phenylglycine); 47931-85-1 (salmon calcitonin); 56-40-6 (Glycine); 61-90-5 (Leucine);

7440-70-2 (Calcium); 9007-12-9 (Calcitonin)
CHEMICAL NAME: 0 (Amino Acids); 0 (Drug Carriers); 0 (Enzyme Inhibitors); 0 (Interferon-alpha); 0 (Trypsin Inhibitors); EC 3.4.11.1 (Leucyl Aminopeptidase); EC 3.4.21.4 (Trypsin)

L18 ANSWER 32 OF 38 MEDLINE on STN
ACCESSION NUMBER: 1999443760 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10512792
TITLE: Dermal and transdermal delivery of protein pharmaceuticals: lipid-based delivery systems for interferon alpha.
AUTHOR: Foldvari M; Baca-Estrada M E; He Z; Hu J; Attah-Poku S; King M
CORPORATE SOURCE: College of Pharmacy and Nutrition, 110 Science Place, University of Saskatchewan, Saskatoon, SK, Canada S7N 5C9.
SOURCE: Biotechnology and applied biochemistry, (1999 Oct) 30 (Pt 2) 129-37.
Journal code: 8609465. ISSN: 0885-4513.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131
Last Updated on STN: 20000131
Entered Medline: 20000119

ABSTRACT:
The dermal and transdermal delivery of protein pharmaceuticals faces enormous challenges, and at the same time has very significant potential for the non-invasive treatment of both localized and systemic diseases. In this article we review the various approaches used to enhance and control the delivery of protein therapeutic agents through the dermal barrier. We show results of the delivery of interferon (IFN) alpha, an antiviral agent used in the treatment of condylomata acuminata (genital warts), using lipid-based delivery systems (LBDS). In the general category of LBDS, we investigated the use of liposomes and fatty acylation as ways to increase IFNalpha delivery into human skin.

CONTROLLED TERM: Check Tags: Human
Acetylation
Administration, Cutaneous
Administration, Topical
***Drug Carriers**
***Drug Delivery Systems**
***Interferon-alpha: AD, administration & dosage**
Interferon-alpha: CH, chemistry
Interferon-alpha: PK, pharmacokinetics
Liposomes
Skin Absorption
CHEMICAL NAME: 0 (Drug Carriers); 0 (Interferon-alpha); 0 (Liposomes)

L18 ANSWER 14 OF 38 MEDLINE on STN
ACCESSION NUMBER: 2003252558 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12659933
TITLE: Biodegradable micro- and nanoparticles as long-term delivery vehicles for interferon-alpha.
AUTHOR: Sanchez Alejandro; Tobio Maria; Gonzalez Libia; Fabra Angels; Alonso Maria J
CORPORATE SOURCE: Department of Pharmacy and Pharmaceutical Technology, School of Pharmacy, University of Santiago de Compostela, 15782, Santiago de Compostela, Spain.
SOURCE: European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences, (2003 Mar) 18 (3-4) 221-9.

Journal code: 9317982. ISSN: 0928-0987.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200401
ENTRY DATE: Entered STN: 20030603
Last Updated on STN: 20040107
Entered Medline: 20040106

ABSTRACT:
The development of new interferon-alpha (IFN-alpha) delivery strategies is a key issue in order to simplify its administration and improve its therapeutic effects, while reducing its dose-related side effects. One of the most attractive approaches towards this aim is the encapsulation of IFN-alpha into poly(lactic-glycolic acid) (PLGA) microspheres. Nevertheless, the stability of IFN-alpha released from these microspheres has been identified as one of the most important concerns in relation to the potential of this approach. Being conscious of this problem, we have used new strategies for the encapsulation of IFN-alpha into biodegradable micro- and nanoparticles. We chose poloxamer 188 as a stabilizing agent and encapsulated IFN-alpha within PLGA/poloxamer blend microspheres prepared by an oil-in-oil solvent extraction technique and also within PLGA micro- and nanospheres containing poloxamer, prepared by the water-in-oil-in-water solvent evaporation technique. The results showed that these techniques led to the efficient encapsulation of IFN-alpha and the modulation of their particle size, ranging from nanospheres (280 nm) to 40 microm-microspheres. These systems exhibit a similar pattern of release that is characterized by an initial burst (2-24% IFN-alpha released, as determined by ELISA) followed by small pulses of immunoenzymatically detected IFN-alpha for up to 1 month. The maintenance of the structural integrity and bioactivity of the protein was confirmed using a cytostasis bioassay. The results showed that the antiproliferative activity of the IFN-alpha varied depending on the formulation. More specifically, PLGA/poloxamer blend microspheres were able to provide significant amounts of active IFN-alpha for up to 96 days. This new IFN-alpha delivery system opens up possibilities to improve present IFN-alpha-based therapies.

CONTROLLED TERM: Check Tags: Human; Support, Non-U.S. Gov't
Biodegradation
Cell Line, Tumor
***Drug Delivery Systems: MT, methods**
***Interferon-alpha: AD, administration & dosage**
*Interferon-alpha: PK, pharmacokinetics
Lactic Acid: AD, administration & dosage
Lactic Acid: PK, pharmacokinetics
*Microspheres
*Nanotubes
Polyglycolic Acid: AD, administration & dosage
Polyglycolic Acid: PK, pharmacokinetics
Polymers: AD, administration & dosage
Polymers: PK, pharmacokinetics
CAS REGISTRY NO.: 26009-03-0 (Polyglycolic Acid); 50-21-5 (Lactic Acid)
CHEMICAL NAME: 0 (Interferon-alpha); 0 (Polymers); 0 (polylactic acid-polyglycolic acid copolymer)

L19 ANSWER 17 OF 18 MEDLINE on STN
ACCESSION NUMBER: 87245715 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3109846
TITLE: Children's respiratory viral diseases treated with interferon aerosol.
AUTHOR: Dai J X; You C H; Qi Z T; Wang X M; Sun P Q; Bi W S; Qian

Y; Ding R L; Du P; He Y
SOURCE: Chinese medical journal, (1987 Feb) 100 (2) 162-6.
Journal code: 7513795. ISSN: 0366-6999.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198708
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 19970203
Entered Medline: 19870817
CONTROLLED TERM: Check Tags: Female; Human; Male
Administration, Inhalation
Aerosols
Animals
Bronchitis: TH, therapy
Child
Infant, Newborn
Influenza: TH, therapy
***Interferon Type I: AD, administration & dosage**
Mumps: TH, therapy
Rabbits
Respiratory Syncytial Viruses
*Respiratory Tract Infections: TH, therapy
*Respirovirus Infections: TH, therapy
CHEMICAL NAME: 0 (Aerosols); 0 (Interferon Type I)

L19 ANSWER 11 OF 18 MEDLINE on STN
ACCESSION NUMBER: 94337513 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8059524
TITLE: [The combined treatment of experimental genital herpes with preparations of interferon and acycloguanosine administered systemically and locally].
Kombinirovannoe lechenie eksperimental'nogo genital'nogo gerpesa preparatami interferona i atsikloguanozina pri sistemnom i mestnom vvedenii preparatov.
AUTHOR: Mel'nikov V R; Kobrinskii G D; Lidak M Iu; Barinskii I F
SOURCE: Voprosy virusologii, (1993 Mar-Apr) 38 (2) 69-71.
Journal code: 0417337. ISSN: 0507-4088.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19940920
Last Updated on STN: 20000303
Entered Medline: 19940915

ABSTRACT:
Combined treatment of experimental genital herpes with liposomal preparations of genetic-engineering alpha 2-interferon (reaferon) and acycloguanosine (acyclovir) was carried out in guinea pigs. The most effective therapeutic action of both preparations was achieved by their parenteral administration. Acyclovir proved to be more effective of the two. No statistically significant differences were observed upon parenteral administration of liposomal and nonliposomal forms of the preparations. The results of the experiments attest to the advantages of treatment of genital herpes by parenteral administration of reaferon and acycloguanosine.

CONTROLLED TERM: Check Tags: Comparative Study; Male
*Acyclovir: AD, administration & dosage
Animals
Drug Carriers
Drug Evaluation, Preclinical

Drug Therapy, Combination
English Abstract
Guinea Pigs
*Herpes Genitalis: DT, drug therapy
Injections, Intramuscular
Injections, Subcutaneous
***Interferon Type I, Recombinant: AD, administration & dosage**
Liposomes
CAS REGISTRY NO.: 59277-89-3 (Acyclovir)
CHEMICAL NAME: 0 (Drug Carriers); 0 (Interferon Type I, Recombinant); 0 (Liposomes); 0 (reaferon)

L19 ANSWER 10 OF 18 MEDLINE on STN
ACCESSION NUMBER: 96010548 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9381878
TITLE: [The clinical efficacy in using leukinferon in adults with diseases caused by the varicella-zoster virus]. Klinicheskaia effektivnost' primeneniia leiinferona u vzroslykh pri zabolevaniiakh, vyzvannykh virusom vetrianoi ospy.
AUTHOR: Kuznetsov V P; Nikolaeva I N; Barer G M; Beliaev D L; Sundukov A V; Babaiants A A; Iushchuk N D
SOURCE: Zhurnal mikrobiologii, epidemiologii, i immunobiologii, (1995 Jul-Aug) (4) 72-5.
Journal code: 0415217. ISSN: 0372-9311.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971125

ABSTRACT:
To achieve more effective treatment of varicella (chickenpox) and herpes zoster in adults, a wide-spectrum immunocorrective agent containing, together with alpha-interferon, a number of other cytokines of the first phase of immune response was used. In patients with the different severity of disease leukinferon induced a rapid decrease in the severity of the disease, arrested the development of new elements on the skin and the buccal mucosa, and reduced the duration of the fever period. When used in such forms as intramuscular injections in combination with the irrigation of the buccal mucosa and ointment, leukinferon proved to be a highly effective preparation for the treatment of diseases caused by varicella-zoster virus.

CONTROLLED TERM: Check Tags: Comparative Study; Human
*Adjuvants, Immunologic: AD, administration & dosage
Administration, Oral
Adolescent
Adult
Aged
*Chickenpox: TH, therapy
*Cytokines: AD, administration & dosage
Drug Combinations
English Abstract
*Herpes Zoster: TH, therapy
Injections, Intramuscular
***Interferon Type I: AD, administration & dosage**
Ointments
Remission Induction
Time Factors

CHEMICAL NAME: 0 (Adjuvants, Immunologic); 0 (Cytokines); 0 (Drug Combinations); 0 (Interferon Type I); 0 (Ointments); 0 (leukinferon)

L19 ANSWER 9 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1998011154 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9350101
TITLE: Human leukocyte interferon-alpha in a hydrophilic cream versus in a gel for the treatment of genital herpes in males: a placebo-controlled, double-blind, comparative study.
AUTHOR: Syed T A; Ahmadpour O A; Ahmad S A; Ahmad S H
CORPORATE SOURCE: Department of Dermatology, University of California, San Francisco 94143-0989, USA.
SOURCE: Journal of dermatology, (1997 Sep) 24 (9) 564-8.
Journal code: 7600545. ISSN: 0385-2407.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122
Last Updated on STN: 20000303
Entered Medline: 19980106

ABSTRACT:
The aim of this double-blind, placebo-controlled, comparative study was to differentiate the clinical efficacy and tolerability of human leukocyte interferon-alpha incorporated (2 x 10(6) IU/g) in a hydrophilic cream and in a gel to heal males afflicted with first episodes of genital herpes. Patients (n = 60), aged 18-40 years (mean 23.2) with culture-confirmed diagnosis of herpes genitalis were randomized to three parallel groups. Each patient was allocated a precoded 40-g tube, containing either preparation or placebo. Cream or gel was applied three times daily for 5 consecutive days. The duration of the active treatment was two weeks. Patients were examined after 48 hours in initial treatment, and thereafter two times a week. A reepithelialized lesion with some residual erythema was recorded as healed. The study demonstrated that patients treated with leukocyte interferon-alpha cream had both significantly shorter mean duration of lesions than gel and placebo recipients (5.3 days vs. 8 days, 13 days respectively; $p < 0.001$) and a higher number of healed patients (80% vs. 55%, 20% respectively; $p < 0.001$). Of the 60 patients, 49 (82%) complained of no drug-related side effects. Eleven patients predominantly in the cream/gel groups reported non-objective transitory increase in their body temperature (> 38 degrees C) with moderate headache, malaise and myalgia. The study was followed-up for 24 months after the first day of the treatment, and out of 31/60 cured patients, 4 had a relapse after 18 months. In conclusion the study affirmed that human leukocyte interferon-alpha (2 x 10(6) IU/g) in a hydrophilic cream is more efficacious than its incorporation in gel or placebo, thus suggesting that leukocyte interferon-alpha in a hydrophilic cream, with a profile of non-objective mild to moderate drug-induced indications, may be considered an alternative and effective treatment modality to cure male patients afflicted with first episodes of genital herpes.

CONTROLLED TERM: Check Tags: Human; Male
Administration, Cutaneous
Adolescent
Adult
Double-Blind Method
Gels
*Herpes Genitalis: TH, therapy
***Interferon Type I, Recombinant: AD, administration &**

dosage
CHEMICAL NAME: 0 (Gels); 0 (Interferon Type I, Recombinant)

L19 ANSWER 7 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1998432953 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9758677
TITLE: Palmitoyl derivatives of interferon alpha: potential for cutaneous delivery.
AUTHOR: Foldvari M; Attah-Poku S; Hu J; Li Q; Hughes H; Babiuk L A; Kruger S
CORPORATE SOURCE: College of Pharmacy and Nutrition, and Veterinary Infectious Disease Organization, University of Saskatchewan, Saskatoon, Saskatchewan, S7N 5C9.. foldvari@duke.usask.ca
SOURCE: Journal of pharmaceutical sciences, (1998 Oct) 87 (10) 1203-8.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981125

ABSTRACT:
Palmitoyl derivatives of interferon alpha2b (p-IFNalpha) were prepared by covalent attachment of the fatty acid to lysine residues in the protein through a reaction with N-hydroxysuccinimide palmitate ester. The p-IFNalpha was characterized by capillary electrophoresis (CE), mass spectrometry (MS), SDS-PAGE, and antiviral assay. Flow-through diffusion cells and human breast skins were used to measure cutaneous and percutaneous absorption. Formation of p-IFNalpha derivatives was demonstrated by CE to be dependent on reaction time and reagent: protein ratio. Electrospray MS of the crude p-IFNalpha mixture indicated three populations of IFNalpha derivatives with 10, 11, and 12 palmitoyl substitutions. The addition of palmitoyl residues to IFNalpha under the conditions described reduced the antiviral specific activity by 50%. However, the cutaneous absorption of p-IFNalpha was about 5-6 times greater than the parent protein. The amount of p-IFNalpha and IFN alpha in whole skin after 24 h of treatment was 2.106 +/- 1.216 microg/cm2 and 0.407 +/- 0.108 microg/cm2, respectively. Approximately two times higher flux was detected for p-IFNalpha compared to the nonfatty acylated IFNalpha. The total amount of drug diffused in 24 h was also approximately two times higher for the p-IFNalpha. The results indicate a potential for using fatty acylated derivatives of IFN alpha for dermal and transdermal delivery.

CONTROLLED TERM: Check Tags: Human; In Vitro
Acylation
Administration, Cutaneous
Amino Acid Sequence
*Antiviral Agents: AD, administration & dosage
Antiviral Agents: CH, chemistry
Drug Carriers
Electrophoresis, Capillary
***Interferon Alfa-2b: AD, administration & dosage**
Interferon Alfa-2b: CH, chemistry
Molecular Sequence Data
*Palmitic Acid: CH, chemistry
Spectrum Analysis, Mass
CAS REGISTRY NO.: 57-10-3 (Palmitic Acid); 99210-65-8 (Interferon Alfa-2b)
CHEMICAL NAME: 0 (Antiviral Agents); 0 (Drug Carriers)

L19 ANSWER 6 OF 18 MEDLINE on STN

ACCESSION NUMBER: 1999293467 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10365133
TITLE: Formulation of interleukin-2 and interferon-alpha containing ultradeformable carriers for potential transdermal application.
AUTHOR: Hofer C; Gobel R; Deering P; Lehmer A; Breul J
CORPORATE SOURCE: Urologische Klinik und Poliklinik, Technischen Universitat Munchen, Germany.
SOURCE: Anticancer research, (1999 Mar-Apr) 19 (2C) 1505-7. Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990714
Last Updated on STN: 20000303
Entered Medline: 19990629

ABSTRACT:
INTRODUCTION: Transfersomes (TF) are new highly deformable hydrophilic lipid vesicles, which are able to spontaneously penetrate the skin barrier because of their characteristics. Transfersomes are able to transport non-invasively low as well as high molecular weight molecules into the body. We describe the formulation and several biological characteristics of Interleukin-2 and Interferon-a containing TF. MATERIAL AND METHODS: TF contain natural phosphatidylcholine and sodium cholate. Recombinant human IL-2 and human hybrid interferon-alpha A/D were added to TF and incubated for 24 hours at 4 degrees C. Immunotransfersomes were isolated from free IL-2 and IFN by filtration (Centrisart, Sartorius). Biological activity of immunotransfersomes was measured by CTLL-cell-assay for IL-2 and by A549--EMCV-assay for IFN, concentrations of proteins by ELISA. RESULTS: It has been possible to incorporate a high amount of IL-2 and IFN in TF (75-80%). Incorporated IL-2 and IFN were biological active. The increase of the proportion of lipid to protein to 90.9/1 led to growing probability of association. CONCLUSION: We were able to show, that IL-2 as well as IFN is trapped by transfersomes in biological active form and in sufficient concentrations for immunotherapy. In upcoming experiments these IL-2 and IFN-containing TF are used for a transdermal approach in the murine RENCA cell line model.

CONTROLLED TERM: Check Tags: Human
Administration, Cutaneous
Biological Assay
Cholic Acid
Drug Carriers
Enzyme-Linked Immunosorbent Assay
Interferon Type I, Recombinant: AD, administration & dosage
***Interferon-alpha: AD, administration & dosage**
*Interleukin-2: AD, administration & dosage
Liposomes
Phosphatidylcholines
Protein Hybridization
Recombinant Proteins: AD, administration & dosage

CAS REGISTRY NO.: 81-25-4 (Cholic Acid)
CHEMICAL NAME: 0 (Drug Carriers); 0 (Interferon Type I, Recombinant); 0 (Interferon-alpha); 0 (Interleukin-2); 0 (Liposomes); 0 (Phosphatidylcholines); 0 (Recombinant Proteins)

L19 ANSWER 3 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2001279276 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11362668
TITLE: Topical interferon for HIV-positive women.
AUTHOR: Anonymous

SOURCE: Positively aware : monthly journal of the Test Positive Aware Network, (1995 Sep-Oct) 5-6.
Journal code: 9413754. ISSN: 1523-2883.
PUB. COUNTRY: United States
DOCUMENT TYPE: (NEWSPAPER ARTICLE)
LANGUAGE: English
FILE SEGMENT: AIDS
ENTRY MONTH: 199509
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20020222
Entered Medline: 19950919

ABSTRACT:
A topical formulation of Interferon alfa-n3 (Alernon N Gel) is in clinical trials for HIV-infected women who are co-infected with human papillomavirus (HPV) and who have persistent cervical dysplasia. A study will compare use of the gel in combination with surgery, versus surgery alone.

CONTROLLED TERM: Check Tags: Female; Human
Administration, Topical
Cervix Dysplasia: ET, etiology
*Cervix Dysplasia: TH, therapy
Gels
*HIV Seropositivity: CO, complications
***Interferon-alpha: AD, administration & dosage**
*Papillomavirus, Human
Papovaviridae Infections: ET, etiology
*Papovaviridae Infections: TH, therapy
Tumor Virus Infections: ET, etiology
*Tumor Virus Infections: TH, therapy

CHEMICAL NAME: 0 (Gels); 0 (Interferon-alpha)

L15 ANSWER 13 OF 15 MEDLINE on STN
ACCESSION NUMBER: 91112217 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2275275
TITLE: [Treatment of experimental genital herpes with liposomal interferon].
Lechenie liposomal'nym interferonom eksperimental'nogo genital'nogo gerpesa.
AUTHOR: Mel'nikov V R; Kobrinskii G D; L'vov N D; Bolotin I M; Barinskii I F
SOURCE: Vestnik Akademii meditsinskikh nauk SSSR, (1990) (8) 35-7.
Journal code: 7506153. ISSN: 0002-3027.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199102
ENTRY DATE: Entered STN: 19910329
Last Updated on STN: 20000303
Entered Medline: 19910226

ABSTRACT:
Treatment of genital herpes was studied in experiments on male guinea pigs infected with herpes simplex II virus in suspension, by means of the penis skin scarification. The medication was provided by interferon (reaferon) prepared by the technique was provided by interferon (reaferon) prepared by the technique of genetic engineering, and incorporated into liposomes composed of phosphatidyl choline and cholesterol (molar ratio, 1:1). Free or liposome-contained interferon solutions, either mixed with hydrocolloidal substance or pure, were applied to the affected site of the animals' genitalia three times daily. The severity of clinical symptoms and disease duration were

used as markers of preparation efficacy. The obtained results showed the liposomal interferon preparations to be most effective irrespective of being mixed with the hydrocolloidal substance or pure. Free interferon solutions demonstrated the lowest therapeutic efficacy, while the effect of hydrocolloidal interferon was found to be median. Experimental use of such antiviral preparations as BIOLF-62 and acyclovir as a medication against genital herpes also showed the advantages of the liposomal drug forms over free solutions.

CONTROLLED TERM: Check Tags: Male
Administration, Cutaneous
Animals
*Balanitis: DT, drug therapy
*Disease Models, Animal
Drug Carriers
Drug Evaluation, Preclinical
English Abstract
Guinea Pigs
*Herpes Genitalis: DT, drug therapy
***Interferon Type I, Recombinant: AD, administration & dosage**
***Liposomes: TU, therapeutic use**

CHEMICAL NAME: 0 (Drug Carriers); 0 (Interferon Type I, Recombinant); 0 (Liposomes); 0 (reaferon)

L15 ANSWER 12 OF 15 MEDLINE on STN
ACCESSION NUMBER: 94360645 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8079531
TITLE: [The use of leukinferon by electrophoresis in children with chronic hepatitis].
Primenenie leikinferona metodom elektroforeza u detei s khronicheskim gepatitom.
AUTHOR: Uchaikin V F; Kuznetsov V P; Cherednichenko T V; Sokolova H V; Syr'eva T N; Chaplygina G V; Konev V A; Iusuf-Zade A A
SOURCE: Zhurnal mikrobiologii, epidemiologii, i immunobiologii, (1993 Nov-Dec) (6) 116-7.
Journal code: 0415217. ISSN: 0372-9311.
PUB. COUNTRY: RUSSIA: Russian Federation
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19941013
Last Updated on STN: 19980206
Entered Medline: 19940930

CONTROLLED TERM: Check Tags: Comparative Study; Human
*Adjuvants, Immunologic: AD, administration & dosage
Child, Preschool
*Cytokines: AD, administration & dosage
Drug Combinations
Drug Evaluation
*Hepatitis B: TH, therapy
*Hepatitis D: TH, therapy
*Hepatitis, Chronic: TH, therapy
Infant
***Interferon Type I: AD, administration & dosage**
***Iontophoresis**
Remission Induction

CHEMICAL NAME: 0 (Adjuvants, Immunologic); 0 (Cytokines); 0 (Drug Combinations); 0 (Interferon Type I); 0 (leukinferon)

L15 ANSWER 10 OF 15 MEDLINE on STN
ACCESSION NUMBER: 96028195 MEDLINE

DOCUMENT NUMBER: PubMed ID: 7473553
TITLE: N-acylated alpha-amino acids as novel oral delivery agents for proteins.
AUTHOR: Leone-Bay A; Santiago N; Achan D; Chaudhary K; DeMorin F; Falzarano L; Haas S; Kalbag S; Kaplan D; Leipold H; +
CORPORATE SOURCE: Emisphere Technologies, Inc., Hawthorne, New York 10532, USA.
SOURCE: Journal of medicinal chemistry, (1995 Oct 13) 38 (21) 4263-9.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19960124
Last Updated on STN: 19990129
Entered Medline: 19951128

ABSTRACT:
A series of N-acylated alpha-amino acids were synthesized and shown to improve the oral delivery of two protein drugs, salmon calcitonin (sCT) and interferon-alpha. Forty-five compounds in this series were tested in vivo in rats and primates. A significant positive correlation was found between the log P of the acylated amino acids and the decrease in serum calcium following oral dosage of sCT in rats. Such a correlation was not found for interferon-alpha. These derivatized amino acids only weakly inhibited the activity of trypsin or leucine aminopeptidase. Histological examinations of rat intestinal tissue after oral dosing of acylated amino acid/protein combinations revealed no detectable pathology.

CONTROLLED TERM: Check Tags: Male
Acylation
*Amino Acids: CH, chemistry
Animals
*Calcitonin: AD, administration & dosage
Calcium: BL, blood
***Drug Carriers**
Enzyme Inhibitors
Glycine: AE, adverse effects
*Glycine: AA, analogs & derivatives
Glycine: CS, chemical synthesis
Glycine: PD, pharmacology
***Interferon-alpha: AD, administration & dosage**
Intestines: AH, anatomy & histology
Intestines: DE, drug effects
Kinetics
Leucine: AE, adverse effects
*Leucine: AA, analogs & derivatives
Leucine: CS, chemical synthesis
Leucine: PD, pharmacology
Leucyl Aminopeptidase: AI, antagonists & inhibitors
Macaca mulatta
Rats
Rats, Sprague-Dawley
Structure-Activity Relationship
Trypsin: ME, metabolism
Trypsin Inhibitors

CAS REGISTRY NO.: 121428-84-0 (N-cyclohexanoylleucine); 28172-57-8 (N-cyclohexanoyl-2-phenylglycine); 47931-85-1 (salmon calcitonin); 56-40-6 (Glycine); 61-90-5 (Leucine); 7440-70-2 (Calcium); 9007-12-9 (Calcitonin)
CHEMICAL NAME: 0 (Amino Acids); 0 (Drug Carriers); 0 (Enzyme Inhibitors); 0 (Interferon-alpha); 0 (Trypsin Inhibitors); EC 3.4.11.1

(Leucyl Aminopeptidase); EC 3.4.21.4 (Trypsin)

L15 ANSWER 7 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1999228811 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10210923
TITLE: Comparative pharmacokinetics and pharmacodynamics of recombinant human interferon beta-1a after intramuscular and subcutaneous administration.
AUTHOR: Rogge M C; Simonian N A; Jones W E
SOURCE: European journal of neurology : official journal of the European Federation of Neurological Societies, (1999 May) 6 (3) 375-7.
Journal code: 9506311. ISSN: 1351-5101.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000706
Last Updated on STN: 20000706
Entered Medline: 20000626
CONTROLLED TERM: Check Tags: Human
***Injections, Intramuscular**
***Injections, Subcutaneous**
***Interferon Type I, Recombinant: AD, administration & dosage**
*Interferon Type I, Recombinant: PK, pharmacokinetics
CHEMICAL NAME: 0 (Interferon Type I, Recombinant)

L15 ANSWER 6 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1999443760 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10512792
TITLE: Dermal and transdermal delivery of protein pharmaceuticals: lipid-based delivery systems for interferon alpha.
AUTHOR: Foldvari M; Baca-Estrada M E; He Z; Hu J; Attah-Poku S; King M
CORPORATE SOURCE: College of Pharmacy and Nutrition, 110 Science Place, University of Saskatchewan, Saskatoon, SK, Canada S7N 5C9.
SOURCE: Biotechnology and applied biochemistry, (1999 Oct) 30 (Pt 2) 129-37.
Journal code: 8609465. ISSN: 0885-4513.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000131
Last Updated on STN: 20000131
Entered Medline: 20000119
ABSTRACT:
The dermal and transdermal delivery of protein pharmaceuticals faces enormous challenges, and at the same time has very significant potential for the non-invasive treatment of both localized and systemic diseases. In this article we review the various approaches used to enhance and control the delivery of protein therapeutic agents through the dermal barrier. We show results of the delivery of interferon (IFN) alpha, an antiviral agent used in the treatment of condylomata acuminata (genital warts), using lipid-based delivery systems (LBDS). In the general category of LBDS, we investigated the use of liposomes and fatty acylation as ways to increase IFNalpha delivery into human skin.
CONTROLLED TERM: Check Tags: Human
Acetylation

Administration, Cutaneous
Administration, Topical
***Drug Carriers**
*Drug Delivery Systems
***Interferon-alpha: AD, administration & dosage**
Interferon-alpha: CH, chemistry
Interferon-alpha: PK, pharmacokinetics
Liposomes
Skin Absorption

CHEMICAL NAME: 0 (Drug Carriers); 0 (Interferon-alpha); 0 (Liposomes)

L15 ANSWER 3 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2000512957 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11071458
TITLE: New ultradeformable drug carriers for potential transdermal application of interleukin-2 and interferon-alpha: theoretic and practical aspects.
AUTHOR: Hofer C; Hartung R; Gobel R; Deering P; Lehmer A; Breul J
CORPORATE SOURCE: Urologische Klinik und Poliklinik, Technischen Universitat Munchen, Germany.. c.hofer@lrz.tu-muenchen.de
SOURCE: World journal of surgery, (2000 Oct) 24 (10) 1187-9. Journal code: 7704052. ISSN: 0364-2313.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

ABSTRACT:
Transfersomes (TFs) are highly deformable hydrophilic lipid vesicles that are able to penetrate the skin barrier spontaneously because of their characteristics. Transfersomes are able to transport noninvasively low- and high-molecular-weight molecules into the body. We describe the formulation and several biologic characteristics of interleukin-2 (IL-2)- and interferon-alpha (IFNalpha)-containing TFs. TFs contain natural phosphatidylcholine and sodium cholate. Recombinant human IL-2 and human hybrid IFNalpha were added to TFs and incubated for 24 hours at 4 degrees C. Immunotransfersomes were isolated from free IL-2 and IFNalpha by filtration (Centrisart, Sartorius). The biologic activity of immunotransfersomes was measured by a cytotoxic lymphoid line assay for IL-2 and by an A549-encephalomyocarditis virus assay for IFN; concentrations of proteins were determined by the enzyme-linked immunosorbent assay (ELISA). It was possible to incorporate a large amount of IL-2 and IFN in TFs (75-80%), and the incorporated IL-2, and IFN were biologically active. The increased lipid/protein ratio (90.9/1.0) led to a growing probability of association. We were thus able to show that IL-2 and IFN are trapped by transfersomes in a biologically active form and in sufficient concentrations for immunotherapy. In upcoming experiments these IL-2- and IFN-containing TFs will be used for a transdermal approach in the murine RENCA cell line model.

CONTROLLED TERM: Check Tags: Human
Administration, Cutaneous
***Drug Carriers**
***Interferon-alpha: AD, administration & dosage**
Interferon-alpha: AN, analysis
*Interleukin-2: AD, administration & dosage
Interleukin-2: AN, analysis
Recombinant Proteins: AD, administration & dosage

CHEMICAL NAME: 0 (Drug Carriers); 0 (Interferon-alpha); 0 (Interleukin-2); 0 (Recombinant Proteins)

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=> fil PASCAL, BIOTECHNO, BIOTECHDS, BIOSIS, CONFSCI
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=> d que l61

L51       74660 SEA INTERFERON#(2A)((TYPE(W)(1 OR I)) OR ALPHA OR BETA OR
                OMEGA OR RECOMBINANT OR ALFA)
L52       11067 SEA OROMUCOS? OR (MOUTH OR ORAL?)(3A)(MUCOUS OR MUCOSA? OR
                TRANSMUCOS?)
L53     1382091 SEA VIRU? OR ANTIVIR? OR VIRAL?
L54      268377 SEA CMV OR HIV OR HSV# OR RHINOVIR?
L55      316242 SEA HEPATITIS(2A)(B OR C OR D) OR MORBILLIVIR? OR CYTOMEGALOVIR
                ? OR PAPILLOMAVIR? OR HERPES?
L56       32626 SEA RHINOVIR? OR VARICELLA? OR DENGUE OR (MEASLES OR MURRAY OR
                JAPANESE OR TICKBORNE OR TICK BORNE)(2A) ENCEPHALITIS
L57        6136 SEA EBOLA OR MARBURG OR LASSA FEVER OR HANTAVIR?
L60        1229 SEA L52(5A)(ADMIN? OR DELIVERY OR DOS#### OR ROUTE#)
L61          26 SEA L51 AND L60 AND (L53 OR L54 OR L55 OR L56 OR L57)


=> fil capl; d que l67

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FILE LAST UPDATED: 3 Aug 2004  (20040803/ED)

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  substance identification.

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L1            19 SEA FILE=REGISTRY ABB=ON  INTERFERON ALPHA?/CN
L2            12 SEA FILE=REGISTRY ABB=ON  INTERFERON BETA?/CN
L3             1 SEA FILE=REGISTRY ABB=ON  "INTERFERON OMEGA (HUMAN)"/CN
L23           24 SEA FILE=CAPLUS ABB=ON  OROMUCOSA?/BI
L24         3800 SEA FILE=CAPLUS ABB=ON  ((ORAL? OR MOUTH)(3A)(MUCOSA? OR
                 MUCOUS?))/BI
L25          217 SEA FILE=CAPLUS ABB=ON  (L1 OR L2 OR L3)
L26        61949 SEA FILE=CAPLUS ABB=ON  INTERFERONS/CT
L27        19183 SEA FILE=CAPLUS ABB=ON  L26(L)(.OMEGA./OBI OR .ALPHA./OBI OR
                 .BETA./OBI)
L28           43 SEA FILE=CAPLUS ABB=ON  (L25 OR L27) AND (L23 OR L24)
L32       156810 SEA FILE=CAPLUS ABB=ON  DRUG DELIVERY SYSTEMS+OLD/CT
L33       130262 SEA FILE=CAPLUS ABB=ON  ADMIN?/OBI OR ROUTE#/OBI
L34           28 SEA FILE=CAPLUS ABB=ON  L28 AND (L32 OR L33)
L35       319076 SEA FILE=CAPLUS ABB=ON  VIRAL?/OBI OR VIRU?/OBI OR ANTIVIR?/OBI

L36        25321 SEA FILE=CAPLUS ABB=ON  HERPESVIR?/OBI OR PAPILLOMAVIR?/OBI
L37         5828 SEA FILE=CAPLUS ABB=ON  RHINOVIR?/OBI OR VARICELLA?/OBI OR
                 DENGUE/OBI OR (MEASLES/OBI OR MURRAY/OBI OR JAPANESE/OBI OR
                 TICKBORNE/OBI OR TICK BORNE/OBI)(L)ENCEPHALITIS/OBI
L38          125 SEA FILE=CAPLUS ABB=ON  MORBILLIVIR?/OBI
L39        24418 SEA FILE=CAPLUS ABB=ON  HEPATITIS/OBI(L)(B/OBI OR C/OBI OR
                 D/OBI)
L40        48177 SEA FILE=CAPLUS ABB=ON  CYTOMEGALOVIR?/OBI OR CMV/OBI OR
                 HIV/OBI
L66         1274 SEA FILE=CAPLUS ABB=ON  EBOLA/OBI OR MARBURG/OBI OR LASSA
                 FEVER/OBI OR HANTAVIR?/OBI
L67           14 SEA FILE=CAPLUS ABB=ON  L34 AND ((L35 OR L36 OR L37 OR L38 OR
                 L39 OR L40) OR L66)


=> fil wpids; d que l65

FILE 'WPIDS' ENTERED AT 11:47:47 ON 04 AUG 2004
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FILE LAST UPDATED:          2 AUG 2004      <20040802/UP>
MOST RECENT DERWENT UPDATE:     200449        <200449/DW>
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    NEW FORMAT GERMAN PATENT APPLICATION AND PUBLICATION
    NUMBERS. SEE ALSO:
    http://www.stn-international.de/archive/stnews/news0104.pdf <<<
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L42        2194 SEA FILE=WPIDS ABB=ON  INTERFERON#(2A)((TYPE(W)(1 OR I)) OR
                ALPHA OR BETA OR OMEGA OR RECOMBINANT OR ALFA)
L43        1296 SEA FILE=WPIDS ABB=ON  OROMUCOS? OR (MOUTH OR ORAL?)(3A)(MUCOUS
                 OR MUCOSA?)
L44       60090 SEA FILE=WPIDS ABB=ON  VIRU? OR ANTIVIR? OR VIRAL?
L45        2071 SEA FILE=WPIDS ABB=ON  RHINOVIR? OR VARICELLA? OR DENGUE OR
                (MEASLES OR MURRAY OR JAPANESE OR TICKBORNE OR TICK BORNE)(2A)E
                NCEPHALITIS
L46       15541 SEA FILE=WPIDS ABB=ON  HEPATITIS(L)(B OR C OR D) OR MORBILLIVIR
                ? OR CYTOMEGALOVIR? OR PAPILLOMAVIR? OR HERPES?
L47       20383 SEA FILE=WPIDS ABB=ON  CMV OR HIV OR HSV# OR RHINOVIR?
L49          86 SEA FILE=WPIDS ABB=ON  (MOUTH OR ORAL?)(3A)TRANSMUCOS?
L64         271 SEA FILE=WPIDS ABB=ON  EBOLA OR MARBURG OR LASSA FEVER OR
                HANTAVIR?
L65          13 SEA FILE=WPIDS ABB=ON  L42 AND (L43 OR L49) AND ((L44 OR L45
                OR L46 OR L47) OR L64)
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=> fil embase; d que l91; d que l100; d que l112

FILE 'EMBASE' ENTERED AT 11:47:49 ON 04 AUG 2004

FILE COVERS 1974 TO 29 Jul 2004 (20040729/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L80        1827 SEA FILE=EMBASE ABB=ON  RECOMBINANT ALPHA INTERFERON/CT
L81       21111 SEA FILE=EMBASE ABB=ON  ALPHA INTERFERON/CT
L82        6680 SEA FILE=EMBASE ABB=ON  BETA INTERFERON/CT
L83          36 SEA FILE=EMBASE ABB=ON  OMEGA INTERFERON/CT
L84      270220 SEA FILE=EMBASE ABB=ON  VIRUS INFECTION+NT/CT
L87        7920 SEA FILE=EMBASE ABB=ON  OROMUCOS? OR (MOUTH OR ORAL?)(3A)(MUCOU
                S OR MUCOSA? OR TRANSMUCO?)
L90         365 SEA FILE=EMBASE ABB=ON  L87(5A)(ADMIN? OR DELIVERY OR DOS####
                OR ROUTE#)
L91           9 SEA FILE=EMBASE ABB=ON  L90 AND (L80 OR L81 OR L82 OR L83) AND
                L84
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L80        1827 SEA FILE=EMBASE ABB=ON  RECOMBINANT ALPHA INTERFERON/CT
L81       21111 SEA FILE=EMBASE ABB=ON  ALPHA INTERFERON/CT
L82        6680 SEA FILE=EMBASE ABB=ON  BETA INTERFERON/CT
L83          36 SEA FILE=EMBASE ABB=ON  OMEGA INTERFERON/CT
L84      270220 SEA FILE=EMBASE ABB=ON  VIRUS INFECTION+NT/CT
L85       73348 SEA FILE=EMBASE ABB=ON  L84(L)(DT OR PC)/CT
L87        7920 SEA FILE=EMBASE ABB=ON  OROMUCOS? OR (MOUTH OR ORAL?)(3A)(MUCOU
                S OR MUCOSA? OR TRANSMUCO?)
L92      440125 SEA FILE=EMBASE ABB=ON  ORAL DRUG ADMINISTRATION/CT
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L100          6 SEA FILE=EMBASE ABB=ON  (L80 OR L81 OR L82 OR L83) AND L92 AND
                L87 AND L85


L54      268377 SEA CMV OR HIV OR HSV# OR RHINOVIR?
L55      316242 SEA HEPATITIS(2A)(B OR C OR D) OR MORBILLIVIR? OR CYTOMEGALOVIR
                ? OR PAPILLOMAVIR? OR HERPES?
L56       32626 SEA RHINOVIR? OR VARICELLA? OR DENGUE OR (MEASLES OR MURRAY OR
                JAPANESE OR TICKBORNE OR TICK BORNE)(2A) ENCEPHALITIS
L57        6136 SEA EBOLA OR MARBURG OR LASSA FEVER OR HANTAVIR?
L80        1827 SEA FILE=EMBASE ABB=ON  RECOMBINANT ALPHA INTERFERON/CT
L81       21111 SEA FILE=EMBASE ABB=ON  ALPHA INTERFERON/CT
L82        6680 SEA FILE=EMBASE ABB=ON  BETA INTERFERON/CT
L83          36 SEA FILE=EMBASE ABB=ON  OMEGA INTERFERON/CT
L84      270220 SEA FILE=EMBASE ABB=ON  VIRUS INFECTION+NT/CT
L85       73348 SEA FILE=EMBASE ABB=ON  L84(L)(DT OR PC)/CT
L93          55 SEA FILE=EMBASE ABB=ON  (L80 OR L81 OR L82 OR L83)(L)PO/CT
L103         10 SEA FILE=EMBASE ABB=ON  L85/MAJ AND L93/MAJ
L111     235486 SEA FILE=EMBASE ABB=ON  (L54 OR L55 OR L56 OR L57)
L112          6 SEA FILE=EMBASE ABB=ON  L103 AND L111
```

DT - drug therapy
PC - prevention
PO - oral administration

```
=> s l91 or l100 or l112

L113         15 L91 OR L100 OR L112

=> fil medl; d que l73; d que l79

FILE 'MEDLINE' ENTERED AT 11:47:50 ON 04 AUG 2004

 FILE LAST UPDATED: 3 AUG 2004 (20040803/UP). FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L4         23492 SEA FILE=MEDLINE ABB=ON  INTERFERON TYPE I+NT/CT
L5        420250 SEA FILE=MEDLINE ABB=ON  C2./CT = Viral Diseases
L6         18339 SEA FILE=MEDLINE ABB=ON  L4(L)(TU OR AD OR PD OR PK)/CT
L68         5785 SEA FILE=MEDLINE ABB=ON  L6 AND L5(L)TH./CT
L69        19643 SEA FILE=MEDLINE ABB=ON  OROMUCOS? OR (MOUTH OR ORAL?)(3A)(MUCO
                 US OR MUCOSA? OR TRANSMUCO?)
L71        73421 SEA FILE=MEDLINE ABB=ON  ADMINISTRATION, ORAL/CT
L73            8 SEA FILE=MEDLINE ABB=ON  L68 AND L71 AND L69
```

TH - therapeutic use
AD - administration & dosage
PD - pharmacology
PK - pharmacokinetics
TH - therapy

```
L4         23492 SEA FILE=MEDLINE ABB=ON  INTERFERON TYPE I+NT/CT
L5        420250 SEA FILE=MEDLINE ABB=ON  C2./CT
L6         18339 SEA FILE=MEDLINE ABB=ON  L4(L)(TU OR AD OR PD OR PK)/CT
L68         5785 SEA FILE=MEDLINE ABB=ON  L6 AND L5(L)TH./CT
L74        15362 SEA FILE=MEDLINE ABB=ON  MOUTH MUCOSA/CT
L78         2029 SEA FILE=MEDLINE ABB=ON  OROPHARYNX/CT
```

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L79             1 SEA FILE=MEDLINE ABB=ON  L68 AND L74 AND L78


=> s l73 or l79

L114            9 L73 OR L79

=> dup rem l114,l61,l67,l113,l65
FILE 'MEDLINE' ENTERED AT 11:48:27 ON 04 AUG 2004

FILE 'PASCAL' ENTERED AT 11:48:27 ON 04 AUG 2004
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PROCESSING COMPLETED FOR L114
PROCESSING COMPLETED FOR L61
PROCESSING COMPLETED FOR L67
PROCESSING COMPLETED FOR L113
PROCESSING COMPLETED FOR L65
L115           51 DUP REM L114 L61 L67 L113 L65 (26 DUPLICATES REMOVED)
                  ANSWERS '1-9' FROM FILE MEDLINE
                  ANSWER '10' FROM FILE PASCAL
                  ANSWERS '11-12' FROM FILE BIOTECHNO
                  ANSWERS '13-23' FROM FILE BIOTECHDS
                  ANSWERS '24-25' FROM FILE BIOSIS
                  ANSWERS '26-37' FROM FILE CAPLUS
                  ANSWERS '38-43' FROM FILE EMBASE
                  ANSWERS '44-51' FROM FILE WPIDS

=> d ibib ab 1-25; d ibib ed ab hitrn 26-37; d ibib ab 38-51; fil hom

L115 ANSWER 1 OF 51     MEDLINE on STN                    DUPLICATE 3
ACCESSION NUMBER:    2002307690     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 12044300
TITLE:               Randomized, double-blind, placebo-controlled trial of
                     oromucosal low-dose interferon following prednisone
                     withdrawal for chronic hepatitis B infection in Filipino
                     patients.
AUTHOR:              Tupasi Thelma E; Co Vilma M; Clarin Ma Socorro M; Alesna
                     Evelyn T; Divinagracia Ella Mae S; Mangubat Nellie V
CORPORATE SOURCE:    Tropical Disease Foundation, Makati Medical Center, Makati
```

City, Philippines.. tdf@info.com.ph
SOURCE: International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases, (2002 Mar) 6 (1) 37-41. Journal code: 9610933. ISSN: 1201-9712.
PUB. COUNTRY: Canada
DOCUMENT TYPE: (CLINICAL TRIAL) Journal; Article; (JOURNAL ARTICLE) (RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 20020611 Last Updated on STN: 20020823 Entered Medline: 20020822

AB OBJECTIVE: To evaluate the efficacy and safety of **oromucosal** low-dose human lymphoblastoid interferon alpha (IFN-alpha-n1 [INS]) following steroid withdrawal in Filipino patients with chronic replicative hepatitis B virus (HBV) infection. STUDY DESIGN: Randomized, double blind, placebo-controlled trial on IFN-alpha-n1 [INS], two tablets of 200 IU each or placebo, given sublingually once daily for eight months following steroid or placebo priming and withdrawal. RESULTS: A statistically significant clearance of hepatitis B e antigen (HBeAg) (50%) and seroconversion to positive antibody to HBeAg (anti-HBe) (42.9%) was noted in those given IFN-alpha-n1 [INS] compared with the placebo group. Clearance of serum HBV-DNA was not significantly different and none cleared HBsAg in both groups. More patients (57%) had normalization of ALT on IFN-alpha-n1 [INS] compared with controls (31.3%). **Oromucosal** IFN-alpha-n1 [INS] was devoid of any evidence of toxicity. CONCLUSION: This study conducted on a limited number of patients demonstrates the potential efficacy of **oromucosal** IFN-alpha-n1 [INS] in chronic HBV infection with therapeutic benefit equal to parenterally administered interferon alpha (IFNalpha) but without the side effects of myelosuppresion. Owing to the small population studied, we are unable to extrapolate these findings to the general population of patients with chronic HBV infection. A large-scale study is needed to confirm these findings.

L115 ANSWER 2 OF 51 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001511393 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11559435
TITLE: Oromucosal interferon therapy: relationship between antiviral activity and viral load.
AUTHOR: Schellekens H; Geelen G; Meritet J F; Maury C; Tovey M G
CORPORATE SOURCE: Department of Medical Microbiology, University of Utrecht, The Netherlands.
SOURCE: Journal of interferon & cytokine research : official journal of the International Society for Interferon and Cytokine Research, (2001 Aug) 21 (8) 575-81. Journal code: 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010918 Last Updated on STN: 20020122 Entered Medline: 20011204

AB Intraperitoneal (i.p.) administration of 20,000 IU recombinant murine IFN-alpha (rMuIFN-alpha) was highly effective in protecting mice challenged i.p. with doses of encephalomyocarditis virus (EMCV) ranging from 44 to 440 LD(50) ($p<0.001$). Oromucosal (o.m.) IFN therapy was also

found to be effective in protecting mice challenged with a lethal dose of EMCV. Thus, 40% of animals infected with 44 LD(50) of EMCV and treated o.m. with 20,000 IU rMuIFN-alpha survived infection with a mean survival time of 12.0 +/- 2.46 days relative to a mean of 6.11 +/- 0.38 days in the control group ($p<0.05$). Oromucosal IFN therapy was found to be ineffective, however, in animals infected with higher doses of EMCV (88-440 LD(50)), even though intraperitoneal administration of the same dose of rMuIFN-alpha resulted in the survival of 90%, 50%, and 60% of animals infected with 88, 220, and 440 LD(50) of EMCV, respectively. These results suggest that oromucosal IFN therapy is effective at relatively low viral load only and that the mechanism of action of oromucosal IFN therapy may be different from that of parenterally administered IFN. Our results suggest that oromucosal IFN therapy may be most effective in chronic viral infections as an alternative to parenterally administered IFN, which is clinically effective but poorly tolerated.

L115 ANSWER 3 OF 51 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1999404580 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10476930
TITLE: Low-dose oral use of interferon inhibits virally induced myocarditis.
AUTHOR: Lawson C M; Beilharz M W
CORPORATE SOURCE: Department of Microbiology, University of Western Australia, Nedlands, Perth.. cassiel@numbat.murdoch.edu.au
SOURCE: Journal of interferon & cytokine research : official journal of the International Society for Interferon and Cytokine Research, (1999 Aug) 19 (8) 863-7.
Journal code: 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 20000111
Last Updated on STN: 20000111
Entered Medline: 19991022

AB Cytomegalovirus (CMV) infection has been associated with the development of myocarditis in humans. Our established mouse model for CMV myocarditis allows detailed investigation of the immunopathogenic mechanisms and therapies for cardiovascular disease. The type I interferons (IFN-alpha/beta) are part of the innate immune response to CMV infections. Previously, we have reported that daily treatment with low doses of murine IFN-alpha/beta administered by the **oral-mucosal** route significantly reduces early virus replication of murine CMV in the spleen and liver of infected mice. The **oral-mucosal** route provides an alternate delivery system to the current modes of IFN administration and is associated with fewer side effects. Since prophylactic treatment with type 1 IFNs may result in both antiviral and immunomodulatory effects that may lessen the development of disease, we wished to study the effect of IFN-alpha/beta on the development of myocarditis. Low-dose oral use of type I IFN (10 IU/day for 7 days prior to virus infection) did not abrogate myocarditis but suppressed the inflammatory response in both the acute and chronic phase of the disease. Furthermore, low-dose oral use of IFN was as effective at inhibiting myocarditis as a single injection of a high dose of IFN (20,000 IU) on the day of virus infection. These findings indicate the need for evaluation of low-dose use of oral IFN in the development of improved clinical therapies for the treatment of cardiovascular disease.

L115 ANSWER 4 OF 51 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1998453064 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9781804
TITLE: **Oral-mucosal** administration of IFN-alpha potentiates immune response in mice.
AUTHOR: Nagao Y; Yamashiro K; Hara N; Horisawa Y; Kato K; Uemura A
CORPORATE SOURCE: Biosciences Research Laboratory, Mochida Pharmaceutical Co., Ltd., Tokyo, Japan.. ynagao@mochida.co.jp
SOURCE: Journal of interferon & cytokine research : official journal of the International Society for Interferon and Cytokine Research, (1998 Sep) 18 (9) 661-6.
Journal code: 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981230

AB We studied the effects of **oral-mucosal** administration of murine interferon-alpha (Mu-IFN-alpha) on immune responses and infection with vaccinia virus (VV) in mice. When Mu-IFN-alpha was administered to sheep red blood cell (SRBC)-sensitized mice for 4 or 5 days, Mu-IFN-alpha significantly enhanced delayed-type hypersensitivity (DTH) and antibody production, with maximum enhancement of each at 1 IU/body. To investigate the antiviral effect of **oral-mucosal** Mu-IFN-alpha, mice were infected with VV, and Mu-IFN-alpha was administered for 15 days. Pocks were observed in the tail skin of infected mice, and Mu-IFN-alpha at doses of 1, 10, and 100 IU/body significantly suppressed pock formation. Also, VV-specific cytotoxic T cells (CTL) were observed in the spleen from the same mice at 7 days after infection, and Mu-IFN-alpha enhanced CTL activity at doses above 1 IU/body. These results suggest that the **oral-mucosal** Mu-IFN-alpha may have potentiating effects on cellular and humoral immune responses, which may contribute to its effects against VV.

L115 ANSWER 5 OF 51 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 94175723 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8129566
TITLE: Treatment of chronic viral hepatitis type B with **oral mucosal** administration of natural human interferon alpha lozenges.
AUTHOR: Caban J; Mossor-Ostrowska J; Zyrkowska-Bieda T; Zejc M; Janas-Skulina U; Ciesla A; Cummins J M; Georgiades J A
CORPORATE SOURCE: Department of the Infectious Diseases, Copernicus Medical School, Cracow, Poland.
SOURCE: Archivum immunologiae et therapiae experimentalis, (1993) 41 (3-4) 229-35.
Journal code: 0114365. ISSN: 0004-069X.
PUB. COUNTRY: Poland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940420
Last Updated on STN: 19980206
Entered Medline: 19940411

AB Results of the administration of natural human interferon alpha (nIFN-alpha) into the oral cavity of 28 patients with chronic aggressive viral hepatitis type B are shown. Diagnosis of chronic aggressive viral hepatitis type B was based on clinical symptoms of disease, histopathological changes as evidenced by liver biopsy and persistence of

HBV markers in patient sera. The daily dose of nIFN-alpha ranged from 75-200 IU/day. The twenty eight patients have been treated for a variable amount of time: thirteen over 300 days, two over 180 days, two over 120 days and eleven for less than 120 days. Only those patients who have been treated for over 300 days are considered to have completed the therapeutical program and remain under observation only. Oral IFN-alpha therapy is safe and efficacious in patients with chronic aggressive viral type B hepatitis. Among these 28 patients, 23 were initially positive for both hepatitis Bs antigen (HBsAg) and hepatitis Be antigen (HBeAg). Eight of these 23 patients have lost HBeAg and developed anti-HBe antibody. In addition one patient from this group seroconverted 356 days after initiation of treatment with IFN-alpha. Three patients lost HBs and HBe antigens and developed antibodies to both HBs and HBe antigens. Two patients who had eliminated HBe antigen before IFN-alpha therapy eliminated HBeAg following treatment and developed antibodies against HBs antigen. Three additional patients initially HBsAg+.HBcAg-, and HBeAg-developed antibody to HBe antigen during IFN-alpha therapy. At the time of this report 12 of the 23 initially viremic patients have seroconverted (52%).(ABSTRACT TRUNCATED AT 250 WORDS)

L115 ANSWER 6 OF 51 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 94175722 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8129565
TITLE: Evaluation of the efficacy of natural human interferon alpha lozenges on the clinical course of childhood neoplasia and in chronic hepatitis B virus infection in patients who were successfully treated for pediatric malignancies.
AUTHOR: Balcerska A; Bohdan Z; Drozynska E; Kozielska E; Szarszewski A; Georgiades J A
CORPORATE SOURCE: Ist and IInd Clinic of Childhood Diseases, Medical Academy, Gdansk, Poland.
SOURCE: Archivum immunologiae et therapiae experimentalis, (1993) 41 (3-4) 221-7.
Journal code: 0114365. ISSN: 0004-069X.
PUB. COUNTRY: Poland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940420
Last Updated on STN: 19940420
Entered Medline: 19940411

AB The immunostimulating and anti-cancer action of interferons (IFNs) has been known for many years. However, IFNs have not been introduced widely into the schemes of oncological treatment because of serious side effects potentiating untoward effects of chemotherapy. In addition using high doses of IFNs by parental routes the cost of such therapy is prohibitively high. Natural human interferon alpha lozenges produced from lymphoblastoid cell line by the Hayashibara Biochemical Lab. Okayama Japan (nHuIFN-alpha, HBL) is used in small doses delivered on **oral mucosa**. Thus, it might be expected not to cause severe side effects, and is less expensive. Children given antineoplastic and immunostimulatory treatment for cancer were also given nHuIFN-alpha--HBL lozenges containing 50-200 units of IFN per lozenge. Children treated age varied from 3-14 years. The average time of observation was 188 days. In 6 patients nHuIFN-alpha therapy was introduced at the time of the intensive oncological treatment during break periods. Those children had advanced malignant solid tumors. For the other children the IFN therapy was used after the successfully completed oncological treatment. The reason of using nHuIFN-alpha in this group was a long lasting hepatitis B

virus antigenemia. The drug was well tolerated by children from both groups and a positive immunostimulating effect was observed. One prominent effect of the nHuIFN-alpha--HBL in children was a reduction of frequency of infections, improvement of appetite and psychological feeling of well being. It seems to us that IFN oral therapy may improve the tolerance of chemotherapy and radiotherapy.

L115 ANSWER 7 OF 51 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 94175721 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7907465
TITLE: An interim report on the effect of natural human interferon alpha (IFN-alpha) lozenges in patients seropositive for the human immunodeficiency virus type 1 (HIV-1).
AUTHOR: Babiuch L; Mian M; Kaminska E; Szymanska B; Georgiades J A
CORPORATE SOURCE: Department of Acquired Immune Deficiency Syndrome, Institute of Infectious and Parasitic Diseases, Warsaw, Poland.
SOURCE: Archivum immunologiae et therapiae experimentalis, (1993) 41 (3-4) 213-9.
Journal code: 0114365. ISSN: 0004-069X.
PUB. COUNTRY: Poland
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940420
Last Updated on STN: 19970203
Entered Medline: 19940411

AB **Oral mucosal** administration of natural human interferon alpha (IFN-alpha) lozenges has previously been applied to the treatment of HIV-1 seropositive patients with benefits including weight gain and amelioration of clinical signs and symptoms of disease. These previous studies have been of short duration and employed treatment at a constant dosage. In this interim report, we describe the positive effects of long-term administration of IFN-alpha lozenges given in increasing dosages over the time. Forty adult patients positive for HIV-1 by ELISA and Western Blot have been enrolled in an ongoing, open-label study. Patients have received IFN-alpha lozenges at dosages ranging from 75-600 IU administered once daily into the oral cavity to promote **oral mucosal** contact. Patients have been treated for variable periods, ranging from 19 days to over 700 days. A group of untreated and unmatched patients, positive for HIV-1 by ELISA and Western Blot, were also followed during this study. At the time of this interim report, only 18 patients had received long-term treatment (more than 168 days with one or more increases in dosage). Five of the 18 patients died; one committed suicide. Two died due to complications of Kaposi sarcoma and another two died of HIV-related causes. The remaining 13 patients have exhibited a significantly smaller mean monthly decrease in CD4+ cells than the untreated but unmatched patients monitored during the same time period (P < or = 0.001).(ABSTRACT TRUNCATED AT 250 WORDS)

L115 ANSWER 8 OF 51 MEDLINE on STN
ACCESSION NUMBER: 2002737634 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12499797
TITLE: **Oromucosal** cytokine therapy: mechanism(s) of action.
AUTHOR: Tovey Michael G
CORPORATE SOURCE: Laboratory of Viral Oncology, UPR 9045 CNRS Institut Andre Lwoff, 94801 Villejuif, France.. tovey@vjf.cnrs.fr
SOURCE: Taehan Kan Hakhoe chi = Korean journal of hepatology, (2002 Jun) 8 (2) 125-31. Ref: 17

Journal code: 9607534. ISSN: 1226-0479.
PUB. COUNTRY: Korea (South)
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200304
ENTRY DATE: Entered STN: 20021227
Last Updated on STN: 20030404
Entered Medline: 20030403

AB **Oromucosal** cytokine therapy allows large amounts of cytokines to be administered with improved outcome and without dose limiting toxicity. Orally administered cytokines exert their effects by a novel two pronged mechanism of action. Firstly, specific populations of immuno-competent effector cells are activated in the oral cavity and migrate to the site of virus replication. Secondly, chemokines produced in the lymphoid tissue of the oral cavity enter the peripheral circulation and redirect activated lymphocytes to eliminate virus infected cells. **Oromucosal** IFN therapy constitutes an alternative and improved means of therapy for diseases such as chronic viral hepatitis which are currently treated parenterally with IFN alpha. The oral route also has obvious advantages for ease of administration and improved patient compliance. Furthermore, the availability of a well tolerated form of IFN therapy will also allow Type I IFNs to be used for the treatment of diseases such as upper respiratory tract virus infections, for which parenteral IFN therapy is currently precluded due to unacceptable toxicity.

L115 ANSWER 9 OF 51 MEDLINE on STN
ACCESSION NUMBER: 90303607 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1973045
TITLE: Low dose oral alpha-interferon therapy for patients seropositive for human immunodeficiency virus type-1 (HIV-1).
AUTHOR: Koech D K; Obel A O; Minowada J; Hutchinson V A; Cummins J M
CORPORATE SOURCE: Kenya Medical Research Institute, Nairobi.
SOURCE: Molecular biotherapy, (1990 Jun) 2 (2) 91-5.
Journal code: 8904897. ISSN: 0952-8172.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 19900921
Last Updated on STN: 19970203
Entered Medline: 19900813

AB Thirty eight symptomatic and two asymptomatic patients seropositive for human immunodeficiency virus type-1 (HIV-1) were treated with a natural human interferon alpha (HuIFN alpha). Patients were given 2 IU/kg HuIFN alpha orally once daily in powdered maltose held in the **mouth** to promote **mucosal** absorption. This oral immunomodulating HuIFN alpha therapy resulted in an increase in CD4+ lymphocytes, an increase in weight, and a dramatic alleviation of clinical symptoms related to HIV-1 infection.

L115 ANSWER 10 OF 51 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED. on STN DUPLICATE 7
ACCESSION NUMBER: 2000-0351097 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2000 INIST-CNRS. All rights reserved.
TITLE (IN ENGLISH): Low-dose oral **interferon-.alpha.**

in the treatment of chronic **viral** hepatitis type B : A double-blind, randomized, placebo-controlled, clinical trial

AUTHOR: YASUDA K.; OHASHI Y.; MATSUSHIMA T.; KUMADA H.; HINO K.; ITO M.; TAKEUCHI T.; KAKUMU S.; KUROKI T.; HAYASHI N.; SATA M.; IINO S.

CORPORATE SOURCE: Research Center for Liver Diseases, Seizankai Kiyokawa Hospital, Tokyo, Japan; Department of Biostatistics, School of Health Sciences and Nursing, University of Tokyo, Tokyo, Japan; Hakodate Municipal Hospital, Hokkaido, Japan; Department of Gastroenterology, Toranomon Hospital, Tokyo, Japan; H.R.I. Ltd., Tokyo, Japan; Department of Internal Medicine, Fujita Health University, School of Medicine, Aichi, Japan; NTT Tokai General Hospital, Aichi, Japan; First Department of Internal Medicine, Aichi Medical University, Aichi, Japan; Third Department of Internal Medicine, Osaka City University Medical School, Osaka, Japan; First Department of Internal Medicine, Osaka University Medical School, Osaka, Japan; Second Department of Internal Medicine, Kurume University, School of Medicine, Fukuoka, Japan; Department of Internal Medicine, Clinical Investigative Medicine, St. Marianna University School of Medicine, Kawasaki, Japan

SOURCE: Current therapeutic research, (2000), 61(5), 245-254, 26 refs.
ISSN: 0011-393X CODEN: CTCEA9

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-9560, 354000088778550010

AB Objective: To assess the efficacy of low-dose oral human interferon-a (LDO-IFN) (MR-22A) in the treatment of chronic **viral** hepatitis type B. Methods: One of 4 doses (single tablet: 50 IU, 150 IU, 450 IU, 900 IU) of MR-22A or a single tablet of placebo was **administered** through the **oral mucosa** once daily for 24 weeks. Results: At the end of the administration period, the proportion of patients who had become hepatitis B **virus** (HBV)-DNA negative was 6 (20.0%) of 30 in the placebo group, 4 (12.9%) of 31 in the 50-IU group, 6 (18.8%) of 32 in the 150-IU group, 2 (6.9%) of 29 in the 450-IU group, and 4 (16.0%) of 25 in the 900-IU group. The proportion of patients who had become hepatitis B e antigen (HBeAg) negative was 5 (17.9%) of 28, 4 (14.8%) of 27, 5 (16.7%) of 30, 4 (14.8%) of 27, and 1 (5.3%) of 19, respectively. None of the differences were statistically significant between the treatment and placebo groups in the proportion of patients who became HBV-DNA negative or HBeAg negative. No statistically significant differences were observed in patients given LDO-IFN or placebo in improvement of liver function. Adverse drug reactions were observed in 4 (12.5%) of 32 patients in the placebo group, 8 (24.2%) of 33 in the 50-IU group, 10 (30.3%) of 33 in the 150-IU group, 10 (29.4%) of 34 in the 450-IU group, and 7 (21.9%) of 32 in the 900-IU group. One patient in the 50-IU group experienced moderate urticaria; all other adverse events were mild. Conclusion: LDO-IFN was not shown to be clinically effective in the treatment of chronic **viral** hepatitis type B with the route of administration, dosing levels, and methods of assessment used in this study.

L115 ANSWER 11 OF 51 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 1999:29109632 BIOTECHNO

TITLE: Oromucosal interferon therapy: Pharmacokinetics and pharmacodynamics
AUTHOR: Eid P.; Meritet J.-F.; Maury C.; Lasfar A.; Weill D.; Tovey M.G.
CORPORATE SOURCE: Dr. M.G. Tovey, CNRS/IFR Y1221, Laboratory of Viral Oncology, 7, rue Guy Moquet, 94801 Villejuif, France. E-mail: tovey@infobiogen.fr
SOURCE: Journal of Interferon and Cytokine Research, (1999), 19/2 (157-169), 25 reference(s)
CODEN: JICRFJ ISSN: 1079-9907
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Oromucosal administration** of .cents.(125)I!-labeled **recombinant** human **interferon-.alpha.**1-8 (IFN-.alpha.1-8), which is biologically active in the mouse, resulted in readily detectable levels of radioactivity in the serum of animals within 5 min. Biologically active IFN could not be detected in the serum at any time after **oromucosal administration**, however, and SDS-PAGE analysis showed that the material present in the serum was of low molecular weight and most probably reflected absorption of degradation products following digestion of IFN in the stomach and small intestine. Furthermore, **oromucosal administration** of murine IFN-.alpha./.beta. (MuIFN.alpha./.beta.) had no significant effect on the expression of IFN-responsive genes in either peripheral blood mononuclear cells or splenic lymphocytes even though in the same animals IFN treatment activated gene transcription locally in the lymphoid tissue of the oropharyngeal cavity and caused a marked systemic **antiviral** activity. **Oromucosal administration** of MuIFN-.alpha./.beta. had no significant effect on either the number of circulating peripheral blood leukocytes or the number of granulocyte-macrophage colonies recovered from the bone marrow of IFN-treated animals. These results suggest that the mechanism of action of oromucosal IFN therapy is distinct from that of parenterally administered IFN and may involve, in the abundant lymphoid or epithelial tissue of the oropharyngeal cavity, either production of a soluble factor or activation of a specific cell population that enters the circulation to mediate the elimination of **virus**-infected or neoplastic cells.

L115 ANSWER 12 OF 51 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN DUPLICATE
ACCESSION NUMBER: 1999:29109631 BIOTECHNO
TITLE: Oromucosal interferon therapy: Marked **antiviral** and antitumor activity
AUTHOR: Tovey M.G.; Maury C.
CORPORATE SOURCE: Dr. M.G. Tovey, CNRS/IFR Y1221, Laboratory of Viral Oncology, 7, rue Guy Moquet, 94801 Villejuif, France. E-mail: tovey@infobiogen.fr
SOURCE: Journal of Interferon and Cytokine Research, (1999), 19/2 (145-155), 33 reference(s)
CODEN: JICRFJ ISSN: 1079-9907
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Oromucosal administration** of murine **interferon-.alpha./.beta.** (IFN-.alpha./.beta.) or individual recombinant species of murine IFN-.alpha., IFN-.beta., or IFN-.gamma. or recombinant human IFN-.alpha.1-8, which is active in the mouse, exerted a marked **antiviral** activity in mice challenged systemically with a lethal

dose of encephalomyocarditis **virus** (EMCV), vesicular stomatitis **virus** (VSV), or **varicella** zoster **virus** (VZV). The effects observed were dose dependent and similar in magnitude to those observed following parenteral administration of the same dose of IFN. No **antiviral** activity was observed after **oromucosal administration** of murine IFN-.alpha./.beta. in animals in which the IFN receptor had been inactivated by homologous recombination. In contrast to parenteral treatment, oromucosal IFN therapy was found to be ineffective when IFNs were **administered** before **virus** infection. **Oromucosal administration** of IFN-.alpha. also exerted a marked antitumor activity in mice injected i.v. with highly malignant Friend erythroleukemia cells or other transplantable tumors, such as L1210 leukemia, which has no known **viral** etiology, the EL4 tumor, or the highly metastatic B16 melanoma. These results show that high doses of IFN can be **administered** by the **oromucosal route** apparently without ill effect, raising the possibility that the **oromucosal route** will prove to be an effective means of administering high doses of IFN that are clinically effective but poorly tolerated.

L115 ANSWER 13 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
DUPLICATE 12
ACCESSION NUMBER: 1995-03231 BIOTECHDS
TITLE: Agent containing interferon(s);
used for protecting bone marrow from inhibition by chemical therapy and radiotherapy
PATENT ASSIGNEE: Toray
PATENT INFO: JP 06298666 25 Oct 1994
APPLICATION INFO: JP 1993-86369 13 Apr 1993
PRIORITY INFO: JP 1993-86369 13 Apr 1993
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
OTHER SOURCE: WPI: 1995-011758 [02]
AB **Interferon-alpha** (IFN-A), **interferon-beta** (IFN-B) and interferon-gamma (IFN-G) are purified from cultured cells or are produced by genetic engineering involving using Escherichia coli, Bacillus subtilis, yeasts and hamster, mouse, monkey, insect or human cells. An IFN gene is introduced into a host cell by using a construct (**virus** or DNA) containing the gene downstream from a promoter which is active in the intended host. An agent containing IFN may be **administered** by injection or taken **orally** or through a **mucous** membrane. The agent protects the bone marrow from inhibition by chemotherapy and radiotherapy and is useful as a protecting or curing agent against a decrease of leukocytes and/or platelets. In an example, mouse IFN was prepared by attaching a methionine codon ATG to the terminal 5' end of part of mouse IFN-B cDNA, which was cloned under the control of the tryptophan promoter in an E. coli plasmid. The vector was introduced into E. coli HB101, which was induced with indoleacrylic acid to accumulate IFN-B. Recombinant IFN-B was purified by silica gel blue, copper chelate and CM-cellulose chromatography. (6pp)

L115 ANSWER 14 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-26447 BIOTECHDS
TITLE: Enhancing an immune response to an antigen, useful for treating or preventing infectious diseases (e.g. **viral**, bacterial or parasitic infections) or cancer, by administering an agent that augments TAP molecule levels in a target cell;
involving **virus** vector plasmid or liposome-mediated gene transfer and expression in host

cell for use in gene therapy
AUTHOR: JEFFERIES W A; ZHANG Q; CHEN S S; ALIMONTI J B
PATENT ASSIGNEE: UNIV BRITISH COLUMBIA
PATENT INFO: US 2003082195 1 May 2003
APPLICATION INFO: US 2002-46542 16 Jan 2002
PRIORITY INFO: US 2002-46542 16 Jan 2002; US 1994-311442 23 Sep 1994
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-743878 [70]
AB DERWENT ABSTRACT:
NOVELTY - Enhancing an immune response to an antigen comprising administering an agent that can augment the level of a TAP molecule (which is a gene located in the major histocompatibility complex (MHC) region that encode proteins of the ATP binding cassette) in a target cell bearing the antigen to a cell or an animal in need of it, is new.
BIOTECHNOLOGY - Preferred Method: The target cell, particularly a tumor cell, is a **virally** infected cell. The method further comprises administering a nucleic acid sequence encoding an antigen, specifically a **viral** antigen or a tumor antigen. The method also includes administering a growth factor, chemokine, accessory molecule or a gene inducible by retinoic acid, tumor necrosis factor, **interferon** (**alpha**, **beta** or gamma), tapasin, calnexin, calreticulin, p53, p58, MHC I heavy chain, HSP 70, HSP 90, BIP, GRB94, or interferon response protein 3 and 7. The accessory molecule consists of tapasin, calnexin, calreticulin, p58, MHC class I heavy chain, beta2M, LMP2 or LMP7. The animal is also subjected to surgery, radiation, chemotherapy, immunotherapy, or photodynamic therapy.
ACTIVITY - Immunostimulant; Cytostatic; **Virucide**; Antibacterial; Antiparasitic. Test details are described but no results are given.
MECHANISM OF ACTION - TAP Agonist; Gene Therapy.
USE - The method is useful for enhancing an immune response to an antigen. The method is particularly useful for treating or preventing infectious diseases (e.g. **viral** infections such as influenza, or bacterial or parasitic infections) or cancer.
ADMINISTRATION - The agent is **administered** intraperitoneally, subcutaneously, intravenously, **orally**, **mucosally**, submucosally, or intradermally (claimed).(70 pages)

L115 ANSWER 15 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-19493 BIOTECHDS
TITLE: New interferon-epsilon polypeptide for diagnosing and treating autoimmune diseases, hepatitis, Parkinson's disease, Alzheimer's disease, cancer or infections (e.g. bacterial or **viral** such as AIDS);
recombinant protein production and its encoding gene for use in gene therapy and diagnosis
AUTHOR: CONKLIN D C; GRANT F J; RIXON M W; KINDSVOGEL W
PATENT ASSIGNEE: ZYMOGENETICS INC
PATENT INFO: US 2003013162 16 Jan 2003
APPLICATION INFO: US 2001-971843 4 Oct 2001
PRIORITY INFO: US 2001-971843 4 Oct 2001; US 1998-101012 18 Sep 1998
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-491969 [46]
AB DERWENT ABSTRACT:
NOVELTY - A new isolated polypeptide (I) comprises an amino acid sequence of: (a) residues 22-192 of a sequence having 192 amino acids (S1) given in the specification; (b) S1, that is at least 70% identical to residues 27-183 of S1; or (c) at least 15 contiguous amino acid residues of S1.
DETAILED DESCRIPTION - A new isolated polypeptide comprises: (a) a first amino acid sequence of residues 22-192 of a sequence having 192

amino acids (S1) given in the specification; (b) a sequence comprising S1 or that is at least 70% identical to residues 27-183 of S1, where the polypeptide specifically binds with an antibody that specifically binds with a polypeptide consisting of S1, or exhibits anti-**viral** activity or anti-proliferative activity; or (c) at least 15 contiguous amino acid residues of S1. INDEPENDENT CLAIMS are included for the following: (1) An isolated nucleic acid molecule that encodes the chimeric interferon-epsilon protein; (2) An expression vector comprising the isolated nucleic acid molecule cited above; (3) A recombinant host cell comprising the expression vector cited above; (4) Using the above expression vector to produce interferon-epsilon protein, comprising culturing the above recombinant host cells that comprise the expression vector and that produce the interferon-epsilon protein; (5) An antibody or antibody fragment that specifically binds with the above polypeptide; (6) A fusion protein comprising an interferon-epsilon moiety; (7) An anti-idiotype antibody, or anti-idiotype antibody fragment, that specifically binds with the above antibody or antibody fragment that possesses anti-**viral** activity or anti-proliferative activity; (8) A recombinant **virus** comprising the above expression vector; (9) A pharmaceutical composition comprising a carrier and the above polypeptide, expression vector, or recombinant **virus** that comprises the vector; and (10) Inhibiting **viral** infection of cells or inhibiting proliferation of tumor cells, comprise administering to the cells the composition comprising the polypeptide or chimeric interferon-i protein, where the chimeric interferon-i protein is characterized by the structure: (hA or mA)-(hAB or mAB)-(hB or mB)-(hBC or mBC)-(hC or mC)-(hCD or mCD)-(hD or mD)-(hDE or mDE)-(hE or mE), where A, B, C, D and E = an interferon-epsilon helix region AB, BC, CD, and DE = an interferon-epsilon loop region h = human interferon-epsilon m = murine interferon-epsilon

WIDER DISCLOSURE - Also disclosed are: (a) methods for detecting the presence of interferon-epsilon RNA in a biological sample; (b) kits for detecting interferon-epsilon polypeptides or nucleic acids; and (c) methods for detecting an alteration in chromosome 9 in the interferon-epsilon gene of an individual.

BIOTECHNOLOGY - Preferred Polypeptide: The isolated polypeptide further comprises a signal secretory sequence that resides in an amino-terminal position relative to the first amino acid sequence, where the signal secretory sequence comprises amino acid residues 1-21 of S1. The polypeptide comprises S1 or a sequence that is at least 80 or 90% identical to the amino acid residues 27-183 of S1. The variant interferon-epsilon polypeptide shares at least 70, 80, 90, 95 or greater than 95% identity to S1, where any difference between the amino acid sequence of the variant polypeptide and that of S1 is due to one or more conservative amino acid substitutions. The sequence of the variant interferon-epsilon polypeptide comprises amino acid residues 22-193 of 2 sequences having 193 amino acids each given in the specification, residues 22-192 of a sequence having 192 amino acids given in the specification, or residues 27-94 of 2 sequences having 208 amino acids each given in the specification, and is characterized by at least one amino acid substitution within an amino acid sequence comprising residues 22-208 of a sequence having 208 amino acids given in the specification selected from an alanine residue for Thr77, a threonine residue for Ser38, a valine residue for Ile90, a glutamic acid residue for Asp23, an aspartate residue for Glu107, and a valine residue for Ile167. The chimeric interferon-epsilon protein has the structure: (mA)-(hAB)-(hB)-(hBC)-(hC)-(mCD)-(mD)-(hDE)-(mE); (mA)-(hAB)-(hB)-(hBC)-(mC)-(hCD)-(hD)-(mDE)-(hE); (mA)-(hAB)-(hB)-(hBC)-(mC)-(hCD)-(mD)-(mDE)-(hE); or (hA)-(mAB)-(mB)-(mBC)-(mC)-(hCD)-(hD)-(mDE)-(hE), where A, B, C, D and E = an interferon helix region AB, BC, CD, and DE = an interferon-epsilon loop region h = human interferon-epsilon m = murine interferon-epsilon The chimeric protein further comprises a signal

sequence located in an N-terminal position, and a human or murine interferon-epsilon C-terminal amino acid sequence. Preferred Nucleic Acid: The nucleic acid molecule comprises a sequence of 576 bp (S2) given in the specification, and remains hybridized following stringent wash conditions to a nucleic acid molecule comprising a sequence of 2313 bp (S3) given in the specification, or its complement. The nucleic acid molecule comprises nucleotides 842-1354 of S3. Preferred Vector: The expression vector comprises the nucleic acid molecule, a transcription promoter, and a transcription terminator, where the promoter is operably linked with the nucleic acid molecule, and the nucleic acid molecule is operably linked with the transcription terminator. The expression vector comprises a murine interferon-epsilon promoter having nucleotides 1-778 of S3. Preferred Antibody: The antibody is a polyclonal antibody, a murine monoclonal antibody, a humanized antibody derived from the murine monoclonal antibody, or a human monoclonal antibody. Preferred Fusion Protein: The fusion protein further comprises an immunoglobulin moiety. Preferred Method: Using the expression vector to produce interferon-epsilon protein, further comprises isolating the interferon-epsilon protein from the cultured recombinant host cells. Preferred Cells: The host cell is selected from a bacterium, yeast, fungal, insect, mammalian and plant cell. Preparation: The polypeptide was prepared using standard isolation and recombinant techniques.

ACTIVITY - Cytostatic; Antibacterial; **Virucide**; Anti-**HIV**; Hepatotropic; Neuroprotective; Nootropic; Antiparkinsonian. No biological data given.

MECHANISM OF ACTION - Gene therapy. No biological data given.

USE - The composition and methods are useful for inhibiting **viral** infection of cells, proliferation of tumor cells (claimed) and in diagnosing and treating a variety of medical conditions, including autoimmune diseases (e.g. multiple sclerosis), hepatitis, Parkinson's disease, Alzheimer's disease, cancers, and infections (e.g. bacterial or **viral** such as AIDS).

ADMINISTRATION - Dosage may range from about 1 pg/kg-10mg/kg of body weight. **Administration** is by **oral**, dermal, **mucosal**-membrane, pulmonary, transcutaneous, intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, intrapleural, intrathecal, by perfusion through a regional catheter, or by direct intralesional injection.

EXAMPLE - No relevant example given. (64 pages)

L115 ANSWER 16 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-08648 BIOTECHDS
TITLE: New HuIFRG 55.1 proteins, useful for preparing a medicament for use in therapy as an anti-**viral**, anti-tumor or immunomodulatory agent, or for treating arthritis, diabetes, lupus, multiple sclerosis, malaria or encephalitis; recombinant protein production and sense and antisense sequence for use in disease gene therapy
AUTHOR: MERITET J; DRON M; TOVEY M G
PATENT ASSIGNEE: PHARMA PACIFIC PTY LTD
PATENT INFO: WO 2002094863 28 Nov 2002
APPLICATION INFO: WO 2002-GB2403 22 May 2002
PRIORITY INFO: GB 2001-12453 22 May 2001; GB 2001-12453 22 May 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-129411 [12]
AB DERWENT ABSTRACT:
NOVELTY - A new isolated polypeptide (I), HuIFRG 55.1, comprises: (a) a fully defined sequence of 490 amino acids (S2) given in the specification; (b) a variant of (a) having substantially similar function of immunomodulatory, **antiviral**, and/or anti-tumor activity; or (c) a fragment of (a) or (b), which retains substantially similar

function of immunomodulatory, **antiviral**, and/or anti-tumor activity.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) A variant or fragment of (I) comprising the amino acid sequence of S2 suitable for raising specific antibodies for the polypeptide and/or its naturally occurring variant; (2) A polynucleotide encoding (I) comprising: (a) a fully defined sequence of 1865 bp (S1) given in the specification, or its coding sequence, and/or a sequence complementary to it; (b) a sequence that hybridizes to the sequence of (a); (c) a sequence that is degenerate as a result of the genetic code to a sequence in (a) or (b); (d) a sequence having at least 60% identity to a sequence in (a), (b) or (c); (e) a polynucleotide that directs expression in vivo of (I); or (f) a polynucleotide capable of expressing in vivo an antisense sequence to a coding sequence for the amino acid sequence of S2 or a naturally occurring variant of the coding sequence for the therapeutic treatment of a human or non-human animal; (3) An expression vector comprising the polynucleotide sequence of (2), which is capable of expressing (I); (4) A host cell containing an expression vector; (5) An antibody specific for (I); (6) A pharmaceutical composition comprising (I) or the polynucleotide of (2), and a carrier or diluent; (7) Producing (I); (8) Identifying (M1) a compound having immunomodulatory activity, **antiviral** activity, and/or anti-tumor activity, comprises providing a cell capable of expressing (I) or its naturally occurring variant, incubating the cell with a compound under test, and monitoring for upregulation of the gene encoding (I) or its variant; (9) A set of primers for nucleic acid amplification, which target sequence within a cDNA; (10) A nucleic acid probe derived from the polynucleotide of (2); (11) Predicting (M2) responsiveness of a patient to treatment with a **Type 1 interferon**, comprises determining the level of the protein having the sequence of S2, or its naturally occurring variant, or the corresponding mRNA, in a cell sample from the patient, where the sample is obtained from the patient following administration of a **Type 1 interferon** or is treated prior to determining with a **Type 1 interferon** in vitro; and (12) A non-human transgenic animal capable of expressing (I).

BIOTECHNOLOGY - Preparation (claimed): Producing (I) comprises culturing the host cells under conditions suitable for obtaining expression of (I), and isolating (I). Preferred Polynucleotide: The polynucleotide is a cDNA. Preferred Probe: The nucleic acid probe is attached to a solid support. Preferred Methods: Predicting responsiveness of a patient to treatment with a **Type 1 interferon**, where the interferon administered prior to obtaining the sample or used to treat the sample in vitro, is the interferon proposed for treating the patient. A sample comprising peripheral blood mononuclear cells isolated from a blood sample of the patient is treated with a **Type 1 interferon** in vitro. The step of determining comprises determining the level of mRNA encoding the protein having the sequence of S2 or its naturally occurring variant.

ACTIVITY - Cytostatic; **Virucide**; Immunosuppressive; Anti-**HIV**; Antiparasitic; Antiarthritic; Antileprotic; Tuberculostatic; Antidiabetic; Antiinflammatory; Neuroprotective; Protozoacide; Dermatological. No biological data given.

MECHANISM OF ACTION - None given.

USE - The polypeptides, polynucleotides encoding the polypeptides, and antibodies are useful for the therapeutic treatment of a human or non-human animal. The polypeptide or polynucleotide is useful for preparing a medicament for use in therapy as an anti-**viral**, anti-tumor or immunomodulatory agent. Administration of (I) or the polynucleotide of (2) is useful for treating a patient having **Type 1 interferon** treatable disease. The methods are also useful for predicting responsiveness of a patient to

treatment with a **Type 1 interferon** (all claimed). Diseases treated include neoplastic diseases such as leukemia, lymphomas or solid tumors, AIDS-related Kaposi's sarcoma, **viral** infections such as chronic hepatitis, autoimmune disease, mycobacterial disease such as leprosy or tuberculosis, parasitic disease, arthritis, diabetes, lupus, multiple sclerosis, malaria, or encephalitis.

ADMINISTRATION - Dosage of HuIFRG 55.1 protein is about 0.1-50 (preferably 0.1-10) mg/kg/day. Dosage of the nucleic acid is about 1 pg to 1 mg, preferably 1 pg to 10 microg. **Administration** may be **oromucosal**, i.e. oral or nasal **route**, intravenous, subcutaneous, intramuscular, or intraperitoneal.

EXAMPLE - No relevant example given. (32 pages)

L115 ANSWER 17 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-04266 BIOTECHDS
TITLE: New compositions comprising CpG-like immunostimulatory nucleic acids, useful for treating or preventing infectious diseases, cancer, allergy, asthma, immunodeficiency, anemia, thrombocytopenia or neutropenia;
oligonucleotide transfer and expression in host cell for immunostimulant and gene therapy
AUTHOR: SCHETTER C; VOLLMER J
PATENT ASSIGNEE: COLEY PHARM GROUP LTD
PATENT INFO: WO 2002069369 6 Sep 2002
APPLICATION INFO: WO 2001-IB2888 10 Dec 2001
PRIORITY INFO: US 2000-254341 8 Dec 2000; US 2000-254341 8 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-723213 [78]
AB DERWENT ABSTRACT:

NOVELTY - Compositions, which comprise a pharmaceutical carrier and an immunostimulatory nucleic acid having a sequence including at least the formula (I), (II) or (III), are new.

DETAILED DESCRIPTION - Compositions comprising an immunostimulatory nucleic acid having a sequence, including at least any one of the following formulae, are new. 5' X1X2CGX3X4 3' (I) 5' X1X2ZYX3X4 3' (II) 5' X1X2C1GX3X4 3' (III). C = methylated; Y = inosine, 2-aminopurine, xanthosine, N7-methyl-xanthosine, nebularine or dSpacer; Z = cytosine, 2'-deoxyuridine (dU), 5-fluoro-2'-dU or dSpacer, and where Z is not cytosine when Y is inosine; C1 = cytosine; I = inosine; and X1, X2, X3 and X4 = nucleotides. An INDEPENDENT CLAIM is also included for a method for inducing an immune response by administering to a subject the novel composition.

BIOTECHNOLOGY - Preferred Composition: The immunostimulatory nucleic acid comprising (I) preferably has a sequence that includes the formula (Ia). The immunostimulatory nucleic acid comprising (II) preferably has a sequence that includes (IIa), and the nucleic acid comprising (III) preferably has a sequence that includes (IIIa). 5' TCNTX1X2CGX3X4 3' (Ia) 5' TCNTX1X2ZYX3X4 3' (IIa) 5' TCNTX1X2C1GX3X4 3' (IIIa). C = 2'-alkoxy cytosine, preferably 2'-methoxy cytosine; N = a nucleic acid sequence composed of 0-25 nucleotides; Z = cytosine, which is unmethylated; and C1 = unmethylated. The immunostimulatory nucleic acid is an isolated nucleic acid, and has 6-100, preferably 8-40, nucleotides. This immunostimulatory nucleic acid has a modified backbone, which a phosphate modified backbone. The immunostimulatory nucleic acid may be a synthetic nucleic acid. Preferably, the immunostimulatory nucleic acid is 18 nucleotides long and is not an antisense nucleic acid. The pharmaceutical carrier is a sustained-release device. The composition further comprises an antigen, an anti-cancer medicament (e.g. a monoclonal antibody, a chemotherapeutic agent or a radiotherapeutic agent), an **antiviral** agent, an antibacterial agent, an antifungal agent, an antiparasitic agent, an ulcer medicament, an allergy medicament, an asthma medicament, an anemia

medicament, a thrombocytopenia medicament, a neutropenia medicament, or a cytokine (e.g. interleukin (IL)-2, IL-3, IL-4, IL-18, **interferon** (IFN)-**alpha**, IFN-gamma, tumor necrosis factor alpha (TNF-alpha), Flt3 ligand, granulocyte colony-stimulating factor (G-CSF), or granulocyte-macrophage colony-stimulating factor (GM-CSF)). Preferably, the composition includes at least two immunostimulatory nucleic acids having different sequences. The composition further comprises a CpG nucleic acid having at least one unmethylated CpG motif. Preferred Method: Inducing an immune response in a subject further comprises administering the antigen (e.g. an allergen, a tumor antigen, a **viral** antigen, a bacterial antigen, a fungal antigen or a parasitic antigen), or the anti-cancer therapy. The immunostimulatory nucleic acid is administered in an amount for stimulating natural killer cell activity.

ACTIVITY - Antimicrobial; Cytostatic; Antiallergic; Antiasthmatic; Immunostimulant; Antianemic; Hemostatic.

MECHANISM OF ACTION - Interleukin-Inducer-1-Beta; Interleukin-Inducer-2; Interleukin-Inducer-6; Interleukin-Inducer-12; Interleukin-Inducer-18; TNF-Inducer-**Alpha**; **Interferon**-Inducer-**Alpha**; **Interferon**-Inducer-Gamma. Peripheral blood monocytes (PBMC) (3x10 to the power 6 cells/ml) obtained from several blood donors were incubated for 8 hours with 6 micro-g/ml of the composition containing oligodeoxynucleotide (ODN) 2006, 2117, 2137, or 1 micro-g/ml lipopolysaccharide (LPS) as positive control. Negative controls were similarly incubated for 8 hours in the absence of added ODN or LPS. After 8 hours, supernatants were collected and IL-1beta (which plays a role in the stimulation of B, T and NK cells, and participates in the conversion of Langerhans cells to professional antigen-presenting dendritic cells, and acts as a chemoattractant for leukocytes) was measured by enzyme linked immunosorbent assay (ELISA). Results showed that CpG ODN were potent inducers of IL-beta secretion.

USE - The compositions are useful for inducing an immune response in a subject, e.g. dog, cat, horse, cow, pig, sheep, goat, rabbit, guinea pig, non-human primate, chicken or fish. The compositions are useful for treating or preventing infectious diseases, cancer, allergy or asthma. The compositions are also useful for enhancing or stimulating bone marrow proliferation in a subject who has or is at risk of developing an immunodeficiency, particularly in a subject undergoing chemotherapy. The compositions are also useful for enhancing erythropoiesis in a subject who has or is at risk of developing anemia, for enhancing thrombopoiesis in a subject who has or is at risk of developing thrombocytopenia, for enhancing neutrophil proliferation in a subject who has or is at risk of developing neutropenia, or for inducing cytokine (e.g. interleukin (IL)-1beta, IL-2, IL-6, IL-12, IL-18, tumor necrosis factor (TNF)-**alpha**, **interferon** (IFN)-**alpha** or IFN-gamma) production. (All claimed).

ADMINISTRATION - Administration is by **mucosal route** (e.g. **oral**, nasal, rectal, vaginal, transdermal or ocular) or parenteral route (e.g. intravenous, subcutaneous, intramuscular or direct injection), or in a sustained-release vehicle (claimed). For mucosal delivery, dosage is 0.1 micro-g-10 mg, preferably 100 micro-g-1 mg/administration, with 2-4 administration spaced days or weeks apart. For parenteral administration, dosage is 10 micro-g-5 mg, preferably 100 micro-g-1 mg/administration, with 2-4 administrations spaced days or weeks apart.

EXAMPLE - No relevant example given. (148 pages)

L115 ANSWER 18 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-02229 BIOTECHDS
TITLE: New **interferon-alpha** induced polypeptide and genes, HuIFRG 15.4, useful in anti-**viral** or anti-tumor therapy, as immunomodulatory agent, or for

treating e.g. neurodegenerative, parasitic or **viral** diseases, tuberculosis or malaria;
recombinant protein and encoded gene or antisense sequence for use in therapy and gene therapy

AUTHOR: MERITET J; DRON M; TOVEY M G
PATENT ASSIGNEE: PHARMA PACIFIC PTY LTD
PATENT INFO: WO 2002062840 15 Aug 2002
APPLICATION INFO: WO 2001-GB2942 29 Jun 2001
PRIORITY INFO: GB 2000-27089 6 Nov 2000; GB 2000-16028 29 Jun 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-643401 [69]

AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide (I) comprising a 131 residue amino acid sequence, given in the specification, its variant having similar function selected from immunomodulatory activity and/or anti-**viral** activity and/or anti-tumor activity, or their fragment which retains the functions, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a variant or fragment of (I) for raising specific antibodies for the polypeptide and/or its naturally-occurring variant; (2) a polynucleotide encoding (I) comprising: (a) a 566 base pair sequence, given in the specification, or a sequence complementary to it; (b) a sequence which hybridizes to (a); (c) a sequence that is degenerate as a result of the genetic code of (a) or (b); (d) a sequence having at least 60 % identity to (a), (b) or (c); (3) an expression vector comprising the polynucleotide capable of expressing the novel polypeptide; (4) a host cell containing the expression vector; (5) an antibody specific for the polynucleotide above; (6) an isolated polynucleotide which directs expression in vivo of (I); (7) a pharmaceutical composition comprising (I) or a polynucleotide of (6), and a pharmaceutical carrier; (8) treating a patient having a **Type 1 interferon** treatable disease by administering (I) or the polynucleotide of (6) to the patient; (9) producing the polypeptides defined above by culturing host cells under conditions to obtain expression of the polypeptide and isolating the polypeptide; (10) identifying a compound having immunomodulatory activity and/or anti-**viral** activity and/or anti-tumor activity by providing a cell capable of expressing (I) or its variant, incubating the cell with a compound under test, and monitoring for upregulation of the gene encoding the polypeptide or variant; (11) a polynucleotide capable of expressing in vivo an antisense sequence to a coding sequence for (I) or a naturally occurring variant of the coding sequence for use in therapeutic treatment of human or non-human animal; (12) a set of primers for nucleic acid amplification which target sequences within a cDNA of the polynucleotide encoding (I); (13) predicting responsiveness of a patient to treatment with **type 1 interferon**; and (14) a non-human transgenic animal capable of expressing (I).

BIOTECHNOLOGY - Preferred Method: Preferred Polynucleotide: The polynucleotide encoding (I) is a cDNA. Preferred Probe: The probe is attached to a solid support. Preferred Method: Predicting responsiveness of a patient to treatment with **type 1 interferon** comprises determining the level of the protein defined the sequence of (I), its naturally occurring variant, or its corresponding mRNA, in a cell from the patient, where the sample is obtained from the patient following administration of a **Type 1 interferon** or is treated before determining **Type 1 interferon** in vitro. The interferon is administered before obtaining the sample or used to treat the sample in vitro. The sample comprises peripheral blood mononuclear cells isolated from a blood sample of the patient is treated with a **type 1 interferon** in vitro. The method also comprises

determining the level of mRNA encoding the protein or its naturally occurring variant.

ACTIVITY - **Virucide**; Cytostatic; Immunomodulator; Immunosuppressive; Neuroprotective; Antiparasitic; Antiinflammatory; Antiarthritis; Antidiabetic; Dermatological; Tuberculostatic; Antileptoric; Protozoacide; Hepatotropic. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The polypeptide or polynucleotide is useful in the therapeutic treatment of human or non-human animal and in preparing a medicament for use in anti-**viral** or anti-tumor therapy, or as immunomodulatory agent. The antibody specific for the polypeptide is also useful for therapeutic treatment. (All claimed). The polypeptide is further useful for treating autoimmune, mycobacterial, neurodegenerative, parasitic or **viral** diseases, arthritis, diabetes, lupus, multiple sclerosis, leprosy, tuberculosis, encephalitis, malaria, cervical cancer, genital **herpes**, **hepatitis B** or **C**, human immunodeficiency **virus** (**HIV**), human papilloma **virus** (HPV), **herpes** simplex **virus** (**HSV**)-1 or 2, or neoplastic disease (e.g. multiple myeloma, cervical cancer or colorectal cancer).

ADMINISTRATION - Dosage is 0.1-50 mg/kg, preferably 0.1-10 mg/kg of HuIFRG 15.4 protein. The nucleic acid is administered at a dose of 1 pg-10 micro-g for particle-mediated gene delivery, and 10 micro-g-1 mg for other routes. Administration can be intradermal, subcutaneous or intramuscular injection.

EXAMPLE - Six week old male DBA/2 mice were treated with either 100000 IU of **recombinant** murine **interferon** **alpha** (IFN **alpha**). After 8 hours, mice were sacrificed by cervical dislocation and the lymphoid tissue was removed surgically from the oropharyngeal cavity. RNA was extracted from the lymphoid tissue and subjected to mRNA differential display analysis using the Message Clean and RNA image kits. Samples were run on 7 % denaturing polyacrylamide gels and exposed to authoradiography. Putative differentially expressed bands were cut out, re-amplified, and used as probes to hybridize Northern blots of RNA extracted from the oropharyngeal cavity of IFN treated, interleukin (IL)-15 treated, and excipient-treated animals. Re-amplified bands from the differential display screen were cloned in the Sfr 1 site of the pPCR-Script (SK(+) plasmid and cDNAs amplified from the rapid amplification of cDNA ends were isolated by Ta cloning in the pCR3 plasmid. DNA was sequenced using an automatic di-deoxy sequencer. Differentially expressed murine 3' sequences identified were compared with random human expressed sequence tags present in the cdEST database of GenBank. Sequences potentially related to the murine expressed sequence tag (EST) isolated from the differential display screen were combined in a contig and used to construct a human consensus sequence corresponding to a putative cDNA. cDNA was found to be 556 nucleotide in length which corresponded to a mouse gene whose expression was enhanced about 5-fold in the lymphoid tissue of the oral cavity of the mice following **oromucosal** **administration** of 1FN-alpha. The cDNA contained an open reading frame of 396 base pairs encoding a protein of 131 amino acids. (33 pages)

L115 ANSWER 19 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-00768 BIOTECHDS
TITLE: Isolated polypeptide, HuIFRG 70, useful for treating **type I interferon** (IFN)-treatable disease e.g., diabetes, leprosy, malaria, colon cancer, lupus and for predicting responsiveness to treatment with IFN-alpha ;

vector-mediated gene transfer, expression in host cell and antibody for recombinant protein production, drug screening and gene therapy

AUTHOR: MERITET J; DRON M; TOVEY M G
PATENT ASSIGNEE: PHARMA PACIFIC PTY LTD
PATENT INFO: WO 2002048182 20 Jun 2002
APPLICATION INFO: WO 2001-GB5496 11 Dec 2001
PRIORITY INFO: GB 2000-30184 11 Dec 2000; GB 2000-30184 11 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-583483 [62]

AB DERWENT ABSTRACT:

NOVELTY - An isolated polypeptide (I) comprising: (a) a fully defined HuIFRG 70 protein sequence (S2); (b) a variant of (S2) having substantially similar function of (S2) such as immunomodulatory activity and/or anti-**viral** activity and/or anti-tumor activity; or (c) a fragment of (a) or (b) which retains a substantially similar function of (S2) as described above, is new.

DETAILED DESCRIPTION - An isolated polypeptide (I) comprises: (a) a fully defined HuIFRG 70 protein sequence of 618 amino acids (S2) as given in specification; (b) a variant of (S2) having substantially similar function of (S2) such as immunomodulatory activity and/or anti-**viral** activity and/or anti-tumor activity; or (c) a fragment of (a) or (b) which retains a substantially similar function of (S2) as described above, where the variant or fragment of (S2) is suitable for raising antibodies for the polypeptide and/or its naturally occurring variant. INDEPENDENT CLAIMS are also included for the following: (1) a polynucleotide (II) encoding (I), where (II) comprises: (a) a fully defined sequence HuIFRG 70 gene (a gene upregulated by administration of **interferon** (IFN)-**alpha**) sequence of 4135 nucleotides (S1) as given in the specification, or its coding sequence and/or complementary sequence; (b) a sequence which hybridizes to (a); (c) a sequence that is degenerate as a result of genetic code to a sequence defined in (a) or (b); or (d) a sequence which has 60% identity to the above mentioned sequences ((II) also directs in vivo expression of (I)); (2) an expression vector (III) comprising (II), which is capable of expressing (I); (3) a host cell (IV) containing (III); (4) an antibody (V) specific for (I); (5) a pharmaceutical composition (VI) comprising (I) or (II) that directs in vivo expression of (I), and a carrier or diluent; (6) preparation of (I); a polynucleotide (VII) capable of expressing in vivo, an antisense sequence to coding sequence for (S2) or a naturally occurring variant of the coding sequence, for use in therapeutic treatment of human or non-human animal; (7) a set of primers for nucleic acid amplification which target sequences within (II), which is preferably a cDNA molecule; (8) a nucleic acid probe derived from (II); and (9) a non-human transgenic animal capable of expressing (I).

BIOTECHNOLOGY - Preparation: (I) is prepared by culturing (IV) such that (I) is expressed and isolated (claimed). Preferred Polynucleotide: (II) is preferably a cDNA molecule. Preferred Probe: The probe is attached to a solid support.

ACTIVITY - Immunosuppressive; Antibacterial; Antiparasitic; **Virucide**; Antiarthritic; Antidiabetic; Dermatological; Antiinflammatory; Neuroprotective; Tuberculostatic; Protozoacide; Cytostatic; Anti-**HIV**. No biological data is given.

MECHANISM OF ACTION - Gene therapy; Immune response modulator; Antisense therapy.

USE - (I) is useful for predicting responsiveness of a patient to treatment with type I IFN which involves determining the level of a protein having a sequence of (S2) or its natural variant, or the corresponding mRNA in cell sample from the patient, where the sample is obtained from the patient following administration of a **type I interferon** or is treated prior to determining with a **type I interferon** in vitro. The IFN administered prior to obtaining the sample or used to treat the sample in vitro is the IFN proposed for treatment of the patient. The sample is

preferably peripheral blood mononuclear cells isolated from blood sample of the patient treated with type I IFN in vitro. The determining step involves determining the level of mRNA encoding the protein defined by (S2) or its naturally occurring variant. (I) or (II) that directs in vivo expression of (I), is useful in therapeutic treatment of a human or non-human animal, and for preparation of medicament for use in therapy as **antiviral**, antitumor or immunomodulatory agent. (I) or (II) that directs in vivo expression of (I), is also useful for treating a patient having a type I IFN treatable disease. (IV) is useful for expressing (I) by recombinant techniques and for identifying a compound having immunomodulatory and/or anti-tumor and/or anti-**viral** activity which involves providing (IV) capable of expressing (S2) or its naturally occurring variant, incubating the cell with a compound and monitoring for upregulation of the gene encoding the polypeptide or variant. (V) is useful for therapeutic treatment. (VII) is useful for treating a human or non-human animal (all claimed). (I) or (II) that directs in vivo expression of (I), is useful for treating a patient having a type I IFN-treatable disease such as autoimmune, mycobacterial, neurodegenerative, parasitic or **viral** disease, arthritis, diabetes, lupus, multiple sclerosis, leprosy, tuberculosis, encephalitis, malaria, cervical cancer, genital **herpes**, **hepatitis** **B** or **C**, human immunodeficiency **virus** (**HIV**), human papilloma **virus** (HPV), **herpes** simplex **virus** (**HSV**)-1 or 2, or neoplastic disease such as multiple myeloma, hairy cell leukemia, carcinoid tumors, cervical cancer, sarcomas including Kaposi's sarcoma, kidney tumors, carcinomas including renal cell carcinoma, hepatic cellular carcinoma, lung cancer, or colon cancer. (II) is useful for producing (I) by recombinant techniques.

ADMINISTRATION - (I) is administered by intravenous route or by infusion. (II) is administered by injection, preferably intradermally, subcutaneously or intramuscularly. Dosage of (I) ranges from 0.1-50 (preferably 0.1-10) mg/kg. Daily dosages of (I) ranges from 5 mg to 2 g. Dosage of (II) ranges from 1 pg to 1 mg, preferably 1 pg to 10 microg nucleic acid for particle-mediated gene delivery and from 10 microg to 1 mg for other routes.

EXAMPLE - Six week old, male DBA/2 mice were treated with either 100000 IU of **recombinant** murine **interferon** **alpha** (IFNalpha) in phosphate buffered saline (PBS), 10 microg of recombinant human interleukin 15 (IL-15), PBS containing 100 microg/ml of bovine serum albumin (BSA), or left untreated. Eight hours later, the mice were sacrificed by cervical dislocation and the lymphoid tissue was removed surgically from the oropharyngeal cavity and snap frozen in liquid nitrogen and stored at -80degreesC. RNA was extracted from the lymphoid tissue by the method of Chomczynski and Sacchi 1987, (Anal.Biochem. 162, 156-159) and subjected to mRNA differential display analysis Lang P. and Pardee, A.B., Science, 257, 967-971. Differentially expressed murine 3' sequences identified from the differential display screen were compared with random human expressed sequence tags (EST) present in the dbEST database of GenBank. The sequences potentially related to the murine EST isolated from the differential display screen were combined in a contig and used to construct a human consensus sequence corresponding to a putative cDNA. One such cDNA was found to be 4135 nucleotides in length. This corresponded to a mouse gene whose expression was found to be enhanced approximately 5-fold in the lymphoid tissue of the oral cavity of mice following **oromucosal** **administration** of recombinant murine IFN-alpha. In order to establish that this putative cDNA corresponded to an authentic human gene, primers derived from the 5' and 3' ends of the consensus sequence were used to synthesize cDNA from mRNA extracted from human peripheral blood leukocytes (PBL) by specific reverse transcription and PCR amplification. A unique cDNA fragment of the predicted size was obtained,

cloned and sequenced. This human cDNA (HuIFRG 70 gene) contains an open reading frame (ORF) of 1857 bp in length at positions 36-1892 encoding a protein of 618 amino acids. Human peripheral blood mononuclear cells (PBMCs) from normal donors were isolated and treated in vitro with 10000 IU of recombinant human IFN-alpha2 in PBA or with an equal volume of PBS alone. Eight hours later the cells were centrifuged and the cell pellet recovered. Total RNA was extracted from the cell pellet and 10.0 microg of total RNA per sample was subjected to Northern blotting in the presence of glyoxal and hybridized with a cDNA probe for HuIFRG 70 mRNA. Enhanced levels of mRNA for HuIFRG 70 protein (approximately 2-fold) were detected in samples of RNA extracted from IFN-alpha treated PBMCs compared to samples treated with PBS alone. (38 pages)

L115 ANSWER 20 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-13566 BIOTECHDS
TITLE: Isolated ATP-dependent interferon responsive protein with immunomodulatory, anti-tumor and/or anti-**viral** activity, useful for treating e.g multiple sclerosis, leprosy, arthritis, encephalitis and lung cancer; vector-mediated recombinant protein gene transfer and expression in host cell, antibody, DNA primer, DNA probe and transgenic animal construction for use in drug screening and autoimmune disease, mycobacterium infection, neurodegenerative disease, parasitic infection, arthritis, diabetes, lupus, multiple sclerosis, leprosy, tuberculosis, encephalitis, malaria, genital **herpes**, **HIV virus** infection, leukemia and cancer therapy
AUTHOR: MERITET J; DRON M; TOVEY M G
PATENT ASSIGNEE: PHARMA PACIFIC PTY LTD
PATENT INFO: WO 2002022682 21 Mar 2002
APPLICATION INFO: WO 2000-GB4139 14 Sep 2000
PRIORITY INFO: GB 2000-25060 12 Oct 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-393947 [42]
AB DERWENT ABSTRACT:
NOVELTY - An isolated ATP-dependent interferon response (HUIFRG46/ADIR) protein (I) comprising one of two fully defined 397 amino acid sequences (S1 and S2) given in the specification; a variant or a fragment of the above, which have immunomodulatory and/or anti-tumor and/or anti-**viral** activity, and is suitable for raising antibodies for (I) and/or its naturally-occurring variant, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a polynucleotide (II) encoding (I), comprising a nucleic acid sequence (NS) of 1285 (S3) nucleotides fully defined in the specification or the coding sequence of (S3) and/or a sequence complementary to (S3); a sequence which hybridizes to S3; a sequence that is degenerate as a result of the genetic code to S3; or a sequence having at least 60% identity to S3; (2) an expression vector (III) comprising (II) which is capable of expressing (I); (3) a host cell (IV) containing (II); (4) an antibody (V) or its fragment which retains antigen-binding capability specific for (I); (5) an isolated polynucleotide (VI) which directs expression in vivo of (I); (6) a pharmaceutical composition comprising (I) or (VI); (7) a product containing both (I) or (VI) and an anti-cancer drug suitable for use as a combined preparation for simultaneous, separate or sequential use in cancer therapy; (8) identifying a compound having immunomodulatory activity and/or anti-**viral** activity and/or anti-tumor activity, involving providing a cell capable of expressing the polypeptide of (S1) or (S2) or its naturally occurring variant, incubating the cell with a compound under test and monitoring for upregulation of the gene encoding the polypeptide or variant; (9) a

polynucleotide (VII) capable of expressing in vivo an antisense sequence to a coding sequence for the amino acid sequence of (S1) or (S2) or a naturally-occurring variant of the coding sequence, for use in therapeutic treatment of a human or non-human animal; (10) a set of primers (VIII) for nucleic acid amplification which target sequences within a cDNA, where the target sequences are part of a sequence of NS; (11) a nucleic acid probe (IX) derived from (II) is suitable for selective detection of a sequence of (NS); and (12) a non-human transgenic animal capable of expressing (I).

WIDER DISCLOSURE - Also disclosed are kits for predicting responsiveness of a patient to treatment with a **Type I interferon**; and labeled and/or immobilized polypeptides packaged in the form of a kit.

BIOTECHNOLOGY - Preparation: Producing (I) involves culturing (IV) under conditions suitable for obtaining expression of (I) and isolating (I) (claimed). Preferred Polynucleotide: (II) is a cDNA. Preferred Probe: (IX) derived from (II) is attached to a solid support.

ACTIVITY - Immunosuppressive; **Virucide**; Antiparasitic; Antiarthritic; Antidiabetic; Neuroprotective: Antileprotic; Tuberculostatic; Antiinflammatory; Protozoacide; Cytostatic; Hepatotropic; Anti-**HIV**; Dermatological.

MECHANISM OF ACTION - Activator of anti-**viral** activity of interferon-2; Apoptosis-Stimulator. The effect of ATP dependent interferon responsive protein (HUIFRG46/ADIR) protein on the human tumor cells was evaluated. Parental HeLa cells or HeLa cells transfected with HuIFRG46/ADIR HAT-PHAT10/11/12 vector expressing the HuIFRG46/ADIR protein were seeded in 96 well microtiter plates at a concentration of 105 cells in Dulbecco's modified eagle medium (DMEM) medium containing 10% fetal bovine serum in the presence or absence of 5 microM 5-fluorouracil (5-FU). Cell proliferation was then followed daily. It was found that the protein induces massive apoptosis of human tumor cells in the presence of 5-FU and all the tumor cells were killed. It was found that 5-FU alone had no significant effect on the apoptosis of human tumor cells and the protein was able to inhibit cell proliferation after 96 hours cultivation of cells. This demonstrated that the antitumor activity of 5-FU was greater in the presence of HuIFRG46/ADIR.

USE - (I) is useful for predicting responsiveness of a patient to treatment with a **Type I interferon**, which involves determining the level of the protein defined by the amino acid sequence of (S1) or (S2) or its naturally-occurring variant or the corresponding mRNA, in a cell sample from the patient, following administration of a **type I interferon**, or is treated prior to the determining with a **Type I interferon** in vitro. The interferon administered prior to obtaining the sample (where the sample comprises peripheral blood mononuclear cells isolated from a blood sample) or used to treat the sample in vitro, is the **Type I interferon** proposed for treatment of the patient. Determining the level of protein comprises determining the level of mRNA encoding the protein defined by the sequence of (S1) or (S2) or a naturally occurring variant of the protein. (I) or (VI) is useful in cancer therapy and in the preparation of a medicament for use in therapy as an anti-**viral**, anti-tumor or immunomodulatory agent. (I), (VI) or (VII) are useful in therapeutic treatment of a human or non-human animal. (I) or (VI) is useful for treating a patient having a **Type I interferon** treatable disease and **viral** disease, and for treating a patient with cancer which involves administering (I) or (VI), optionally in combination with an anti-cancer drug. (V) is useful in therapeutic treatment. (X) is useful for selective detection of (NS) (claimed). (II) is useful in producing HUIFRG 46/ADIR protein. (VII) is useful in treatment of diseases associated with upregulation of HuIFRG46/ADIR protein. (VIII) or (IX) are useful in identifying mutations in

HuIFRG46/ADIR genes for e.g. single nucleotide polymorphisms. (V) is useful in a purification, isolation or screening method and as a tool to elucidate the function of the protein or its variant. (I) is useful in treating **Type I interferon** treatable diseases such as autoimmune, mycobacterial, neurodegenerative, parasitic or **viral** disease, arthritis, diabetes, lupus, multiple sclerosis, leprosy, tuberculosis, encephalitis, malaria, cervical cancer, genital **herpes**, **hepatitis B** or **C**, human immunodeficiency **virus** (**HIV**), human papilloma **virus** (HPV), **herpes** simplex **virus** (**HSV**)-1 or 2, or neoplastic disease such as multiple myeloma, hairy cell leukemia, sarcomas including Kaposi's sarcoma, and carcinomas including lung cancer and renal cell carcinoma.

ADMINISTRATION - (I) is administered by oral or intravenous routes and (VI) is administered by intradermal, subcutaneous, intramuscular, intranasal or oral routes or by particle-mediated gene delivery. Dosage of (I) is preferably 0.1 mg-10 mg/kg of body weight daily and (VI) is preferably 1 pg-10 microg for particle-mediated gene delivery and 10 microg-1 mg for other routes.

EXAMPLE - Six week old, male DBA/2 mice were treated with **recombinant** murine **interferon alpha** (IFNalpha) in phosphate buffered saline (PBS). Eight hours later the mice were sacrificed and the lymphoid tissue was removed surgically and snap frozen in liquid nitrogen and stored at -80degreesC. RNA was extracted from the lymphoid tissue and subjected to mRNA differential display analysis Lang, P., and Pardec, A.B., Science, 257, 967-971. Differentially expressed murine 3' sequences identified from the differential display screen were compared with random human expressed sequence tags (EST). The sequences potentially related to the murine EST isolated from the differential display were combined in a contig and used to construct a human consensus sequence corresponding to a putative cDNA. A full length cDNA was then generated by reverse transcriptase (RT) polymerase chain reaction (PCR) from RNA extracted from Daudi cells cloned and sequenced. The human cDNA was found to be 1285 nucleotides in length, which corresponded to the mouse gene whose expression was found to be enhanced approximately 5-fold in the lymphoid tissue of mice following **oromucosal administration** of IFN-alpha. A unique cDNA fragment of the predicted size was obtained, cloned and sequenced (a sequence of 1285 nucleotides fully defined in the specification). This human cDNA contained an open reading frame (ORF) of 1194 nucleotides in length at positions 74-1267 encoding a protein of 397 (S1) amino acids with a molecular weight of 46 nDa and localized on human chromosome 1. The human and mouse cDNA sequences exhibited 85% identity and the proteins which they code were 70% identical and display similar features such as a hydrophobic N-terminal sequence and an ATP binding domain with typical A, B and Box IV motifs. They also had eight conserved potential phosphorylation sites and an N-glycosylation site. A number of different clones were obtained and were sequenced. The majority had a sequence of 1285 (S2) and some had an alternative 1285 (S3) nucleotide sequence fully defined in the specification and differed from (S2) at position 110 and 1256. The protein encoded by (S3) had a sequence of 397 amino acids fully defined in the specification and differed from (S1) at position 13 and 395. The putative mouse interferon sensitive response element (ISRE) was not identified in the human gene in the promoter region. The ATP-binding domain in ATP dependent interferon responsive (HuIFRG46)/ADIR protein allowed the protein to play a role in apoptosis which was important in antitumor activity and in **antiviral** activity of the interferons. (71 pages)

L115 ANSWER 21 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-09997 BIOTECHDS
TITLE: Novel cytoplasmic, nuclear, membrane bound and secreted NOVX

polypeptides, useful for treating developmental disorders, endocrine disorders, vascular disorders, infectious diseases and neurodegenerative disorders;
vector-mediated recombinant protein gene transfer and expression in host cell for use in gene therapy

AUTHOR: RASTELLI L; SHIMKETS R A; ZERHUSEN B; MALYANKAR U M; PADIGARU M
PATENT ASSIGNEE: CURAGEN CORP
PATENT INFO: WO 2002006329 24 Jan 2002
APPLICATION INFO: WO 2000-US22709 18 Jul 2000
PRIORITY INFO: US 2000-221650 28 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-179781 [23]

AB DERWENT ABSTRACT:
NOVELTY - An isolated NOVX polypeptide (I), comprising a sequence (S1) of 1247, 602, 200, 756, 757, 341, 350, 249 or 791 amino acids fully defined in the specification, is new.

DETAILED DESCRIPTION - An isolated NOVX polypeptide (I), comprising a sequence (S1) of 1247, 602, 200, 756, 757, 341, 350, 249 or 791 amino acids fully defined in the specification, is new. (I) is selected from NOV1, NOV2, NOV3, NOV4a, NOV4b, NOV5a, NOV5b, NOV6 and NOV7 polypeptides, and they are related to NOPE, cadherin, **interferon alpha**-13, ADAM, ankyrin repeat-containing, transpanin and semaphorin polypeptides, respectively. (I) comprises an amino acid sequence selected from: (a) a mature form of S1; (b) a variant of S1 or the mature form, where one or more amino acid residues in the variant differs from S1 or the amino acid sequence of the mature form, provided that the variant differs in no more than 15% of the amino acid residues of S1 or the mature form; or (c) the amino acid sequence of S1. INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule (II) comprising: (a) a nucleic acid sequence encoding (I); (b) a nucleic acid fragment encoding at least a portion of a polypeptide comprising S1 or its variant as described above; or (c) a nucleic acid sequence comprising a complement of the above polynucleotides; (2) a vector (III) comprising (II); (3) a cell (IV) comprising (III); (4) an antibody (Ab) that immunospecifically binds to (I); (5) a method of determining the presence or amount of (I) in a sample, comprising contacting the sample with Ab, and determining the presence or amount of Ab bound to the polypeptide, therefore determining the presence or amount of (I) in the sample; (6) a method (M1) of determining the presence or amount of (II) in a sample, comprising contacting the sample with a probe that binds to (II); and determining the presence or amount of the probe bound to the nucleic acid; (7) a method (M2) of identifying an agent that binds to (I), comprising contacting the polypeptide with the agent and determining whether the agent binds to the polypeptide; (8) a method for identifying an agent that modulates the expression or activity of (I), comprising providing a cell expressing the polypeptide, contacting the cell with the agent, and determining whether the agent modulates expression or activity of the polypeptide, where an alteration in expression or activity of the peptide indicates the agent modulates expression or activity of the polypeptide; (9) a method for modulating the activity of (I), comprising contacting a cell sample expressing (I) with a compound that binds to the polypeptide in an amount sufficient to modulate the activity of the polypeptide; (10) a method of treating or preventing a NOVX-associated disorder, comprising administering to a subject in which such treatment or prevention is desired, (I), Ab or (II) in an amount sufficient to treat or prevent the NOVX-associated disorder in the subject; (11) a pharmaceutical composition (PC) comprising (I), (II) or Ab; (12) a kit comprising PC; and (13) a method for determining the presence of or predisposition to a disease associated with altered levels of (I), preferably cancer, in a

first mammalian subject, comprising: (a) measuring the level of expression of the polypeptide in a sample from the first mammalian subject; and (b) comparing the amount of the polypeptide in the sample of step (a) to the amount of polypeptide present in a control sample from a second mammalian subject known not to have, or not to be predisposed to the disease, where an alteration in the expression level of the polypeptide in the first subject as compared to the control sample indicates the presence of or predisposition to the disease; (14) a method for determining the presence of or predisposition to a disease associated with altered levels of (II), preferably cancer, in a first mammalian subject, comprising: (a) measuring the amount of the nucleic acid in a sample from the first mammalian subject; and (b) comparing the amount of the nucleic acid in the sample of step (a) to the amount of the nucleic acid present in a control sample from a second mammalian subject known not to have, or not to be predisposed to the disease, where an alteration in the expression level of the nucleic acid in the first subject as compared to the control sample indicates the presence of or predisposition to the disease; (15) treating a pathological state in a mammal, by administering a polypeptide having at least 95% identity to S1, or its biologically active fragments; and (16) a method of treating a pathological state in a mammal, comprising administering Ab in an amount that is sufficient to alleviate the pathological state.

WIDER DISCLOSURE - The following are disclosed: (1) NOVX chimeric or fusion proteins; (2) identifying specific cell or tissue types based on their expression of a NOVX; (3) novel agents identified by the above said screening assays; (4) an isolated antisense nucleic acid molecule hybridizable or complementary to a sequence (S2) comprising 3740, 1857, 632, 2439, 2434, 1069, 1222, 758 or 2390 nucleotides fully defined in the specification, or its fragment, analog or derivatives; (5) determining NOVX protein, nucleic acid expression or activity in an individual to select appropriate therapeutic or prophylactic agents for that individual; and (6) monitoring the influence of agents on the expression or activity of NOVX in clinical trials.

BIOTECHNOLOGY - Preparation: (I) is produced by standard recombinant techniques. Preferred Polypeptide: (I) comprises the sequence of a naturally occurring allelic variant which comprises a sequence that is the translation of a nucleic acid sequence differing by a single nucleotide from a sequence (S2) comprising 3740, 1857, 632, 2439, 2434, 1069, 1222, 758 or 2390 nucleotides fully defined in the specification. The sequence of the variant comprises a conservative amino acid substitution. Preferred Polynucleotide: (II) comprises S2, a nucleotide sequence differing by one or more nucleotides from S2, provided that no more than 20% of the nucleotides differ from S2, or its fragment. (II) hybridizes under stringent conditions to S2 or its complement. Alternately, (II) comprises a first nucleotide sequence comprising a coding sequence differing by one or more nucleotide sequences from the coding sequence encoding S1, its complement or fragment. (III) further comprises a promoter operably linked to (II). Preferred Antibody: Ab is a monoclonal or humanized antibody. Preferred Method: In M1, the presence or amount of the nucleic acid molecule is used as a marker for cell or tissue type. The cell or tissue type is cancerous. In M2, the agent is a cellular receptor or a downstream effector.

ACTIVITY - Antiinflammatory; hemostatic; immunosuppressive; cytostatic; metabolic; nootropic; neuroprotective; antiparkinsonian; hepatotropic; vulnerary; antibacterial; gynecological; **virucide** ; antiparasitic; antithyroid; hypotensive; antiinfertility; cerebroprotective; vasotropic; antianemic; antirheumatic; antiarthritic; tranquilizer; antiarteriosclerotic. No biological data given.

MECHANISM OF ACTION - Gene therapy; modulator of NOVX; vaccine. No biological data given.

USE - (I) is useful for identifying an agent (a cellular receptor or downstream effector) that binds to (I), or an agent that modulates the

expression or activity of (I). (I), (II) and Ab are useful for treating or preventing NOVX-associated disorders in humans (all claimed).(I), (II) and Ab are useful in the manufacture of a medicament for treating developmental, endocrine, vascular, gastrointestinal, lungs, respiratory, inflammatory, blood, reproductive, hematopoietic, neurodegenerative, and autoimmune and immune disorders, infectious diseases, cancers, anorexia, Alzheimer's disease, Parkinson's disease, multiple sclerosis, hepatitis, trauma, **viral**, bacterial, parasitical infections, hyperthyroidism, hypothyroidism, endometriosis, fertility, angiogenesis, hypertension, stroke, ischemia, arteriosclerosis, aneurysms, Bare lymphocytic syndrome, hereditary spherocytosis, hemolytic anemia, Werner syndrome, juvenile rheumatoid arthritis, Grave's disease, wound healing, X-linked metal retardation, psychotic and neurological disorders, and neuronal degeneration, and other disorders related to cell signal processing and metabolic pathway modulation. (I) and (II) are useful in diagnostic applications. Fragments of (II) are useful as hybridization probes. (IV) is useful for producing non-human transgenic animals. (I) is useful as bait proteins in two hybrid or three hybrid assay to identify other proteins that bind to or interact with (I). (II) is useful for producing (I), chromosome mapping, for identifying individual, minute biological, sample (tissue typing), and in forensic assay identification of biological sample.

ADMINISTRATION - PC is **administered** through parenteral, **oral**, transdermal, **transmucosal** or rectal **route**. **Dosage** not specified.

EXAMPLE - No relevant example is given.(178 pages)

L115 ANSWER 22 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2003-00541 BIOTECHDS
TITLE: Dual phase polymeric composition, useful for controlled release of an agent over a prolonged period of time, comprises a continuous biocompatible gel phase and microparticles containing the agent;
polymer-mediated gene transfer and expression in host cell for drug delivery and gene therapy
AUTHOR: SHIH C; ZENTER G
PATENT ASSIGNEE: MACROMED INC
PATENT INFO: US 2002076441 20 Jun 2002
APPLICATION INFO: US 2001-906041 13 Jul 2001
PRIORITY INFO: US 2001-906041 13 Jul 2001; US 2000-559507 27 Apr 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-582915 [62]
AB DERWENT ABSTRACT:

NOVELTY - A dual phase polymeric agent-delivery composition comprises a continuous biocompatible gel phase, a discontinuous microparticulate phase and an agent to be delivered contained at least in the microparticulate phase.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for: (1) a method for delivering an agent in a controlled manner over a prolonged period of time comprising administration of the composition as a suspension with subsequent gel formation in response to a stimulus; (2) a method for delivering an agent in a controlled manner over a prolonged period of time comprising administration of the gelled composition; and (3) a method for enhancing the stability of a drug during release from a microparticle delivery system by use of the composition.

ACTIVITY - None given in source material.

MECHANISM OF ACTION - None given in source material.

USE - The composition is useful for controlled release over a long period of time of the agent with enhanced stability of the agent (claimed).

ADMINISTRATION - Preferably parenterally, ocularly, topically, by

inhalation, transdermally, vaginally, buccally, **transmucosally**, transurethrally, rectally, nasally, **orally** or by pulmonary or aural **routes** (claimed).

EXAMPLE - Zn-hGH was incorporated into poly(D,L-lactide-co-glycolide) microspheres. The microspheres (10 mg) were suspended in a reverse thermal gellation solution (20% in 10 mM HEPES buffer, pH7.0, 100 microl). The gel was then set at 37 degrees C and a dissolution medium (100 mM HEPES, pH7.4 with 0.02% Tween-20, 1 ml) was added and the release profile was monitored. The novel composition released less than 25% of the agent in 6 days compared to 80% in the first day in the absence of the reversed thermal gellation agent. (12 pages)

L115 ANSWER 23 OF 51 BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2002-06956 BIOTECHDS
TITLE: New composition, useful for treatment and/or prophylaxis of cancer and tumor, comprises immunostimulatory molecule and animal cells cultured in presence of interferon to enhance antigen presenting function of the cells;
cell culture, interferon and vector expression in host cell for disease therapy and immunostimulant
AUTHOR: RALPH S J
PATENT ASSIGNEE: UNIV MONASH
PATENT INFO: WO 2001088097 22 Nov 2001
APPLICATION INFO: WO 2000-AU565 17 May 2000
PRIORITY INFO: AU 2000-7553 17 May 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-082990 [11]
AB DERWENT ABSTRACT:

NOVELTY - A composition of matter (I) comprising an immunostimulatory molecule and animal cells cultured in the presence of at least one interferon (IFN) for a time and under conditions sufficient to enhance the antigen presenting function of the cells, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) enhancing (M1) immunopotentiation of animal cells comprising: (a) culturing animal cells expressing an immunostimulatory membrane molecule in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the cells; or (b) culturing animal cells in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the cells, and combining the cells so cultured with an immunostimulatory molecule in soluble form; (2) enhancing (M2) or otherwise improving the immunogenicity of an antigen comprising providing animal cells cultured in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the cells and loading the antigen onto the IFN-treated animal cells; (3) a composition of matter (II) for eliciting an immune response against a target antigen, comprises animal cells cultured in the presence of at least one IFN for a time under conditions sufficient to enhance the antigen presenting functions of the cells, where an antigen corresponding to target antigens has been loaded onto IFN-treated animal cells; (4) a vaccine (III) for stimulating a host's immune system, comprises (I) or (II); (5) a kit (IV) comprising (I); (6) assessing (M3) the responsiveness of animal cells to treatment with at least one IFN comprising detecting in the animal cells the level and/or functional activity of a polypeptide involved in interferon signaling, a modulatory agent that modulates the polypeptide, or a downstream cellular target of the polypeptide, or the level of an expression product of a genetic sequence encoding the polypeptide, the modulatory agent or the downstream cellular target; (7) use of a target cell (V) in an assay for detecting cytolytic activity of a cytotoxic T lymphocyte (CTL) for the target cell, where the target cell has been cultured in the presence of at least one

IFN for a time and under conditions sufficient to enhance the antigen presenting function of the cell; (8) detecting (M4) CTL mediated lysis of a target cell comprising providing a target cell in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the target cells, contacting the target cell with a CTL that has cytolytic activity for the target cell and detecting CTL-mediated lysis of the target cell; and (9) use of an antigen binding molecule that is immuno-interactive with a polypeptide or modulatory agent, or a detector polynucleotide or oligonucleotide that hybridizes to the expression product in a kit for assessing the responsiveness of animal cells to treatment with at least one IFN.

BIOTECHNOLOGY - Preferred Composition: In (I), the immunostimulatory molecule is a T cell co-stimulatory molecule selected from B7 molecule (preferably B7-1 or B7-2 molecule) and an intracellular adhesion molecule (ICAM) (preferably ICAM-1 or ICAM-2 molecule). The B7-1 molecule comprises a sequence of 288 amino acids fully defined in the specification, or a biologically active fragment, variant or derivative of the sequence, or comprises a sequence of 229 or 233 amino acids fully defined in the specification. The B7-2 molecule comprises a sequence of 323 amino acids fully defined in the specification, or a biologically active fragment, variant or derivative of the sequence. The immunostimulatory molecule is present in a soluble form. The soluble B7 molecule is a chimeric protein comprising a polypeptide corresponding to the extracellular domain of a B7 molecule fused or otherwise linked to an immunoglobulin constant region. The immunostimulatory molecule is an immunostimulatory membrane molecule of the cells, where at least a portion of the molecule is exposed to the extracellular environment. The animal cells are inactivated cancer or tumor cells derived from a tissue, organ or system selected from lung, breast, uterus, cervix, ovaries, colon, pancreas, prostate, testes, stomach, bladder, kidney, bone, liver, the reticuloendothelial system, esophagus, brain, skin and soft tissues. The cancer or tumor cells are selected from melanoma cells and mammary carcinoma cells. The cells have been cultured in the presence of an IFN-gamma and optionally one or both of a first type I IFN and a second type I IFN, where the first type I IFN is selected from IFN-beta, or its biologically active fragment, variant or derivative, and an analog of IFN-beta, and the second **type I interferon** is selected from IFN-alpha, or its biologically active fragment, variant or derivative, and an analog of IFN-alpha. The IFN-gamma comprises a sequence of 166 amino acids fully defined in the specification. IFN-beta is IFN-beta 1 which comprises a sequence of 187 amino acids fully defined in the specification, or IFN-beta 2 which comprises a sequence of 212 amino acids fully defined in the specification. IFN-alpha comprises a sequence of 188 amino acids fully defined in the specification. The IFN-alpha is IFN-alpha 1 which comprises a sequence of 189 amino acids fully defined in the specification, or IFN-alpha 2 which comprises the sequence of 188 amino acids fully defined in the specification. The type II IFN is an IFN gamma and the type I IFN is selected from IFN-alpha and IFN-beta. The cells are cultured in the presence of a type II IFN from about 16-96 hours and subsequently in the presence of at least one type I IFN from about 16-72 hours. The cells are cultured in the presence of IFN-alpha from about 48-96 hours and subsequently in the presence of IFN-alpha and/or IFN-beta from 24-72 hours. Preferred Method: M1 further comprises isolating cells expressing the immunostimulatory membrane molecule from a heterogeneous population of animal cells, and modifying the animal cells to express the immunostimulatory membrane molecule by introducing into the animal cells a polynucleotide from which the immunostimulatory membrane molecule is expressed, and inactivating the cells by treating the cells to render them incapable of proliferation. In M2, the animal cells are cultured by contacting the cells with a type II IFN for a time and under conditions sufficient to permit cellular responsiveness to at least one type I IFN and then contacting the

cultured cells with the at least one type I IFN for a time and under conditions to enhance the antigen presenting function of the cells. M2 further comprises inactivating the cells by treating the cells to render them incapable of proliferation. In M3, the antigen is of **viral**, bacterial, fungal or protozoal origin. In M3, the polypeptide is signal transducer and activator of transcription I (StatI). M4 further comprises culturing the target cell in the presence of at least one IFN for a time and under conditions sufficient to enhance the antigen presenting functions of the target cell. Preferred Cell: (V) expresses an immunostimulatory membrane molecule, and is contacted with the CTL, preferably CD8+ CTL, in the presence of a soluble immunostimulatory molecule.

ACTIVITY - Cytostatic; antitumor; antibacterial; **virucide**; fungicide; protozoacide.

MECHANISM OF ACTION - Vaccine; enhancer of antigen presenting function of cells (claimed). Preclinical trials were conducted using immunopotentiating composition as a cancer vaccine. Treatment of cells with gamma interferon (IFN) for 72 hours and beta-IFN for 48 hours was shown to optimally induce increased levels of surface expression of major histocompatibility complex (MHC) class I on melanoma cells, particularly on human melanoma cells. Levels of intracellular adhesion molecule (ICAM)-1 and B7 antigens on the human cells were also elevated by IFN treatment. However, given the common loss of B7 expression on these cells, the immunopotentiating composition included transfection to express B7-1 antigen. The transfected B7 expressing murine melanoma cells were shown to be unaltered in their responses to the optimal IFN treatment showing similar strong inductions of MHC class I antigen. Results from studies with the B16 melanoma model showed that the expression of B7-1 and IFN treatment were important for producing CD8 positive cytotoxic T lymphocytes (CTLs) with potent cytolytic activity against B16 cancer cells and that these cells were capable of lysing target cells even though they did not express B7 antigen. Given the level of immunity shown to be induced by the B7Hi interferon treated B16 cells measured by cytotoxicity assay, the same cell preparations were tested for their ability to induce anti-cancer immunity in whole animals when injected as a vaccine. The protocol compared the use of B7Hi/B16 transfected cells to vaccination with wild type B16 cells. The cells were irradiated and cohorts of mice were vaccinated by intraperitoneal injection weekly for up to six weeks. Vaccinated mice were challenged at week 7 with an injection subcutaneously on the rear flank with 5 x 10 to the power of 5 B7Med B16 cells. The results showed that all twenty control animals receiving only the challenge cancer cells succumbed to a 2 cm tumor growth by day 38. However, mice vaccinated with the B7Hi interferon treated immunopotentiating composition produced the greatest resistance to the challenge with 90% surviving with no sign of tumor and continued to remain tumor free thereafter. Thus, it was concluded that the B7Hi/IFN treated immunopotentiating composition induced potent CD8 positive CTL responses and were capable of providing sufficient immunity to protect the majority of vaccinated mice from the cancer cells.

USE - (I) or (III) is useful for treatment and/or prophylaxis of a disease or condition, such as tumorigenesis, by administering (I) or (III) to the patient. (I) which comprises the soluble immunostimulatory molecule and the cultured animal cells is administered separately, sequentially or simultaneously to the patient (claimed). (I) or (V) is useful for treatment and/or prophylaxis of cancer. (I), (II) or (V) is useful for treating **viral**, bacterial, fungal and protozoal infections.

ADMINISTRATION - (I) is **administered** by **oral**, rectal, **transmucosal**, intestinal, systemic, local or parenteral **route** (including intramuscular, subcutaneous, intramedullary, intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal or intraoccular route) at a dose of 1-2000

mg/day, preferably 10-150 mg/day.

EXAMPLE - Melanoma cell line B16 alone or transduced with a vector expressing murine B7-1 was grown in RPMI 1640 media supplemented with 10% v/v inactivated fetal calf serum (FCS), L-glutamine and sodium pyruvate at 37 degrees C in a 5% v/v CO2 incubator. A four hour 51Cr release cytotoxic T cell assay was carried out using the B16 mouse melanoma cell line as targets or alternatively, transfected B16 cells expressing B7-1. The targets were set up at a sub-confluent state, 60 hrs before the cytotoxic T lymphocyte (CTL) assay. Within 12 hours of setting up the cells in culture, murine interferon gamma at 1000 IU/mL was added, followed by an addition of murine **interferon beta** at 1000 IU/mL 24 hours later. A standard chromium release assay was carried out where the targets were labeled with 150 micro Ci/mL Na251CrO4 for 60-90 minutes and used to incubate with cultured splenocytes for 4 hours at 37 degrees C, 5% CO2. CTL lysis was determined at effector:target (E:T) ratios ranging from 100:1 to 0.4:1 to 0.4:1. Supernatants (50 micro liter/sample) were harvested and counted using a scintillation cocktail in a top count using a 96 well plate format. Supernatants were also counted directly using a gamma counter, and specific lysis was calculated. (127 pages)

L115 ANSWER 24 OF 51 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5

ACCESSION NUMBER: 2001:463545 BIOSIS
DOCUMENT NUMBER: PREV200100463545
TITLE: Effect of **oromucosal administration** of IFN-alpha on allergic sensitization and the hypersensitive inflammatory response in animals sensitized to ragweed pollen.
AUTHOR(S): Meritet, Jean-Francois; Maury, Chantal; Tovey, Michael G. [Reprint author]
CORPORATE SOURCE: Laboratory of Viral Oncology, CNRS - UPR 9045, Institut Andre Lwoff, 7, Rue Guy Moquet, 94801, Villejuif, France tovey@vjf.cnrs.fr
SOURCE: Journal of Interferon and Cytokine Research, (August, 2001) Vol. 21, No. 8, pp. 583-593. print. ISSN: 1079-9907.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Oct 2001
Last Updated on STN: 23 Feb 2002

AB **Oromucosal** (o.m.) **administration** of **interferon -alpha** (IFN-**alpha**) during either allergic sensitization (days 0-6) or the hypersensitive response (days 11 and 12) or both periods caused a dose-dependant reduction in allergen-specific IgE production and allergen-induced eosinophil recruitment in mice sensitized to ragweed pollen, a common allergen in humans. Treatment during the hypersensitive response period alone appeared to be most effective. Oromucosal treatment was as effective as intraperitoneal (i.p.) treatment, with maximum inhibition of both allergen-specific IgE production and allergen-induced eosinophil recruitment observed at a dose of a 1000 IU IFN-alpha. Treatment of animals with up to 105 IU murine IFN-alpha/beta (MuIFN-alpha/beta) by either the om. or i.p. route did not inhibit significantly allergen-specific IgG production, which may even have been increased at certain doses of IFN. Treatment of animals with up to 105 IU MuIFN-alpha/beta by either the o.m. or i.p. route did not affect significantly total serum IgE or IgG levels. **Oromucosal administration** of IFN-alpha reduced allergen-specific IgE production and allergen-induced eosinophil recruitment in the absence of detectable toxicity, the induction of H2 antigen expression, and 2',5'-oligoadenylate synthetase activity associated with parenteral administration of IFN-alpha and thus may find application for the

treatment of asthma and associated **viral** infections.

L115 ANSWER 25 OF 51 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:58387 BIOSIS
DOCUMENT NUMBER: PREV199800058387
TITLE: **Oral-mucosal administration** of murine IFN alpha potentiates immune response in mice.
AUTHOR(S): Nagao, Yuji; Yamashiro, Kazuya; Hara, Noriko; Horisawa, Yoshifumi; Kato, Katsuaki; Uemura, Akio
CORPORATE SOURCE: Biosciences Res. Lab., Mochida Pharmaceutical Co. Ltd., 1-1-1 Kamiya, Kita-ku, Tokyo 115, Japan
SOURCE: Journal of Interferon and Cytokine Research, (Oct., 1997) Vol. 17, No. SUPPL. 2, pp. S109. print.
Meeting Info.: Annual Meeting of the International Society for Interferon and Cytokine Research. San Diego, California, USA. October 19-24, 1997. International Society for Interferon and Cytokine Research.
ISSN: 1079-9907.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Jan 1998
Last Updated on STN: 30 Jan 1998

L115 ANSWER 26 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:875046 CAPLUS
DOCUMENT NUMBER: 139:345961
TITLE: Methods and apparatus for modifying properties of the BBB and cerebral circulation by using the neuroexcitatory and/or neuroinhibitory effects of odorants on nerves in the head
INVENTOR(S): Shalev, Alon
PATENT ASSIGNEE(S): Brainsgate Ltd., Israel
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003090599	A2	20031106	WO 2003-IL338	20030425

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-376048P P 20020425
US 2003-461232P P 20030408

ED Entered STN: 07 Nov 2003
AB A method for modifying a property of a brain in a patient includes

presenting an odorant to an air passage of the patient, the odorant having been selected for presentation to the air passage to increase conductance of mols. from a systemic blood circulation of the patient through a blood brain barrier (BBB) of the brain into brain tissue of the patient. The mols. are selected from the group consisting of: apharmacol. agent, a therapeutic agent, an endogenous agent, and an agent for facilitating a diagnostic procedure.

L115 ANSWER 27 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2003:376551 CAPLUS
DOCUMENT NUMBER: 138:367598
TITLE: Topical use of cytokines and chemokines for the treatment of **viral** or mycotic skin diseases or tumoral diseases
INVENTOR(S): Nieland, John; Rehfuess, Christoph
PATENT ASSIGNEE(S): Medigene Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039444	A2	20030515	WO 2002-EP12438	20021107
WO 2003039444	A3	20031113		
WO 2003039444	B1	20031218		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10154579	A1	20030528	DE 2001-10154579	20011107
EP 1441755	A2	20040804	EP 2002-796544	20021107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

PRIORITY APPLN. INFO.: DE 2001-10154579 A 20011107
WO 2002-EP12438 W 20021107

ED Entered STN: 16 May 2003
AB The invention relates to the use of at least one cytokine and/or chemokine in the prodn. of a topically acting medicament for treating viral and/or mycotic skin diseases and/or tumoral diseases. The topical medicament also contains adjuvants as well as emulsifiers.

L115 ANSWER 28 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2001:221884 CAPLUS
DOCUMENT NUMBER: 134:221458
TITLE: Therapeutic applications of high dose interferon
INVENTOR(S): Tovey, Michael Gerard
PATENT ASSIGNEE(S): Pharma Pacific Pty Ltd., Australia
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6207145	B1	20010327	US 1997-853870	19970509
US 6660258	B1	20031209	US 1998-169844	19981009
US 2003108519	A1	20030612	US 2002-330311	20021230
PRIORITY APPLN. INFO.:			AU 1996-9765 A	19960509
			AU 1996-3959 A	19961203
			AU 1996-4387 A	19961224
			US 1997-853292 A2	19970509
			US 1997-853293 A2	19970509
			US 1997-853870 A2	19970509
			FR 1997-12687 A	19971010
			US 1999-243030 A3	19990203

ED Entered STN: 29 Mar 2001

AB Cancer or viral infections can be treated by **oromucosal** administration of interferons, generally at dosages greater than 20X106 IU but less than 1000x106.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L115 ANSWER 29 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 16

ACCESSION NUMBER: 1989:160390 CAPLUS

DOCUMENT NUMBER: 110:160390

TITLE: Disease treatment by contacting interferon with **oral** and pharyngeal **mucosa** and low-dose pharmaceuticals therefor

INVENTOR(S): Cummins, Joseph M.

PATENT ASSIGNEE(S): Amarillo Cell Culture Co., Inc., USA

SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803411	A1	19880519	WO 1987-US2998	19871106
W: AU, BB, BG, BR, DK, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO, SD, SU				
RW: AT, BE, BJ, CF, CG, CH, CM, DE, FR, GA, GB, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 1320905	A1	19930803	CA 1987-550816	19871102
ZA 8708295	A	19880629	ZA 1987-8295	19871105
AU 8812227	A1	19880601	AU 1988-12227	19871106
AU 625431	B2	19920709		
EP 341258	A1	19891115	EP 1988-901169	19871106
EP 341258	B1	19940302		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 102047	E	19940315	AT 1988-901169	19871106
DK 8803743	A	19880905	DK 1988-3743	19880705
DK 172974	B1	19991025		
NO 8802983	A	19880906	NO 1988-2983	19880705
NO 176995	B	19950327		
NO 176995	C	19950705		
US 5019382	A	19910528	US 1990-465527	19900117
AU 9226345	A1	19921203	AU 1992-26345	19921009
US 5830456	A	19981103	US 1994-305418	19940913
US 6372218	B1	20020416	US 1995-381136	19950131
US 5817307	A	19981006	US 1995-484376	19950607

US 5824300	A	19981020	US 1995-479958		19950607
US 5846526	A	19981208	US 1995-476621		19950607
US 5882640	A	19990316	US 1995-475753		19950607
PRIORITY APPLN. INFO.:			US 1986-927834	A	19861106
			US 1987-110501	A	19871026
			EP 1988-901169	A	19871106
			WO 1987-US2998	A	19871106
			US 1991-775291	B1	19911009
			US 1992-875071	B1	19920428
			US 1993-3624	B1	19930113
			US 1993-9353	B1	19930126
			US 1994-305418	A3	19940913

ED Entered STN: 30 Apr 1989

AB Interferon (I) is used to treat autoimmune disorders characterized by a tissue degenerative condition. I is brought into contact with the **oral** and pharyngeal **mucosa** at doses of 0.022-11 IU/kg/day. A patient suffering from malignant melanoma was treated orally with I and after 6 mo was free of the disease. A mouthwash contained 850 mL PBS, 100 mL glycerol, 50 g dextrose, and 0.3 mL of a mixt. of flavor oils, 30 mL surfactant soln., and 50 mL PBS contg. 120 IU I/mL; the formulation contains 120 IU I/20 mL. The patient is asked to hold 20 mL of mouthwash in his/her mouth, optionally gargling with the same, for a period of 15 s to 1 min.

L115 ANSWER 30 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:198252 CAPLUS
DOCUMENT NUMBER: 140:259056
TITLE: Drug delivery systems including carrier proteins for enhancing sorption via skin and mucous membrane
INVENTOR(S): Hofschneider, Peter Hans; Podschun, Trutz; Hildt, Eberhard
PATENT ASSIGNEE(S): Procom Biotechnologische Produktions G.m.b.H., Germany
SOURCE: Ger. Offen., 19 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10240894	A1	20040311	DE 2002-10240894	20020904
WO 2004022657	A1	20040318	WO 2003-EP9788	20030903
WO 2004022657	C1	20040422		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2002-10240894 A 20020904

ED Entered STN: 11 Mar 2004

AB The invention concerns drug delivery systems that contain coupled carrier proteins for enhancing drug penetration through skin and mucous membranes; the peptide PLSSIFSRIGDP is conjugated to interferon, a virus, or a virus-like particle. Transdermal or trans-mucosal prepns. are formulated. A .beta.-interferon-carrier peptide fusion was expressed, purified and

incubated with human hepatoma cell line; cell fractions were isolated and proteins isolated by SDS-PAGE; the fusion protein was detected in contrary to .beta.-interferon that did not carry the peptide.

L115 ANSWER 31 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:319255 CAPLUS
DOCUMENT NUMBER: 138:343854
TITLE: Buccal sprays or capsules containing drugs for treating disorders of the central nervous system
INVENTOR(S): Dugger, Harry A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 537,118.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077227	A1	20030424	US 2002-230060	20020829
WO 9916417	A1	19990408	WO 1997-US17899	19971001
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 1029536	A1	20000823	EP 2000-109347	19971001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EP 1036561	A1	20000920	EP 2000-109357	19971001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2004035021	A2	20040429	WO 2003-US26847	20030827
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004141923	A1	20040722	US 2003-671720	20030929
US 2004120895	A1	20040624	US 2003-726585	20031204

PRIORITY APPLN. INFO.:		
WO 1997-US17899	A2	19971001
US 2000-537118	A2	20000329
EP 1997-911621	A3	19971001
US 2002-230060	A	20020829

ED Entered STN: 25 Apr 2003
AB Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biol. active compds. for rapid absorption through the **oral mucosa**, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation A: aq. polar solvent, active compd., and optional flavoring agent; formulation B: aq. polar solvent, active compd., optionally flavoring

agent, and propellant; formulation C: non-polar solvent, active compd., and optional flavoring agent; and formulation D: non-polar solvent, active compd., optional flavoring agent, and propellant. Thus, a lingual spray contained sumatriptan succinate 10-15, EtOH 10-20, propylene glycol 10-15, PEG 35-40, water 10-15, and flavors 2-3%.

L115 ANSWER 32 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:120230 CAPLUS
DOCUMENT NUMBER: 138:248484
TITLE: Method and means for stimulation of resistance to infection
INVENTOR(S): Grigoryan, S. S.; Ershov, F. I.
PATENT ASSIGNEE(S): Russia
SOURCE: Russ., No pp. given
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2191594	C1	20021027	RU 2001-108756	20010403
PRIORITY APPLN. INFO.:			RU 2001-108756	20010403

ED Entered STN: 16 Feb 2003
AB Method and means are disclosed for stimulation of resistance to infection. Method involves administeration of sublingual granules each contg. interferon at the dose 2000-4000 MU and base. As the base prepn. contains saccharose and lactose. The prepn. is administeres sublingually according to the scheme: 5 granules 1-3 times daily 30 min before meals for 10-15 days. Method involves administeration of new interferon prepn. in the form of sublingual granules contg. low doses of reaferon or realderon or interferon inductor (ridostine, larifan, poludan, amixine, neovir, cycloferon, kagocel, dibasol, papaverine, caffeine, kurantil, and others). The other feature involves increasing resistance to viruses or other infectious agents like influenza, parainfluenza viruses, enteroviruses, adenoviruses, herpes simplex viruses, Epstein-Bar viruses, coronaviruses, rhinoviruses, respiratory syncytial viruses, chlamydias, mycoplasms. Method ensures the enhanced effectiveness in stimulating immunity in protection of **oral** and nasopharyngeal **mucous** membranes, and underlining tissues.

L115 ANSWER 33 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:101000 CAPLUS
DOCUMENT NUMBER: 134:152656
TITLE: Use of histamine as a drug delivery enhancing compound for use in transmucosal or transdermal delivery
INVENTOR(S): Senior, Judy
PATENT ASSIGNEE(S): Maxim Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001008706	A1	20010208	WO 2000-US20757	20000728

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1229939 A1 20020814 EP 2000-955284 20000728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1999-146641P P 19990730
WO 2000-US20757 W 20000728

ED Entered STN: 09 Feb 2001

AB A transmucosally administrable compn. with enhanced penetration comprising: about 0.001-25% of a permeation enhancing agent selected from the group consisting of histamine, histamine dihydrochloride, histamine phosphate, a pharmaceutically acceptable salt thereof, other histamine agonists, about 0.2-90% of a pharmaceutically active medicament, about 0-99.8 % of solvent, and about 0-50% of a gelling agent. For example, a transmucosal patch comprising an ED of insulin and 0.1% (by wt.) of histamine dihydrochloride was prepd. and applied to buccal mucosa. The histamine dihydrochloride present in the patch was transferred by diffusion from the patch to the mucosa. Mols. of insulin also passed into the mucosa and then into the blood stream of the subject wearing the transmucosal patch. The histamine dihydrochloride enhanced the delivery of the insulin into the subject's blood stream.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L115 ANSWER 34 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:98581 CAPLUS
DOCUMENT NUMBER: 132:150598
TITLE: Stereoisomers of CpG oligonucleotides and related methods
INVENTOR(S): Krieg, Arthur M.
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA; CPG Immunopharmaceuticals, Inc.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006588	A1	20000210	WO 1999-US17100	19990727
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2333854	AA	20000210	CA 1999-2333854	19990727
AU 9953238	A1	20000221	AU 1999-53238	19990727
AU 764532	B2	20030821		
EP 1100807	A1	20010523	EP 1999-938843	19990727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1998-94370P P 19980727
WO 1999-US17100 W 19990727
OTHER SOURCE(S): MARPAT 132:150598
ED Entered STN: 11 Feb 2000
AB The interactions of nucleic acids with proteins can be selective for the R stereoisomer, the S stereoisomer, or can be stereoindependent. The present invention demonstrates that the S stereoisomer of CpG contg. DNA is active in mediating the immune stimulatory effects of CpG DNA. The invention provides methods of use of a pure stereoisomer or of DNA enriched for this form for clin. applications for CpG DNA, such as vaccine adjuvants, immune activators for the prevention or treatment of retroviral, viral, parasitic or fungal diseases, or cancer immunotherapy, immunotherapy of allergic and asthmatic diseases, etc. The invention also provides methods of use for R stereoisomer DNA to oppose the immune stimulatory effects of CpG DNA. Such R stereoisomers are useful in the treatment of diseases such as Sepsis syndrome, intestinal inflammatory diseases, psoriasis, gingivitis, systemic lupus erythematosus and other autoimmune diseases.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L115 ANSWER 35 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:265913 CAPLUS
DOCUMENT NUMBER: 130:301711
TITLE: **Oromucosal** cytokine compositions for use as immunostimulants
INVENTOR(S): Tovey, Michael Gerard
PATENT ASSIGNEE(S): Pharma Pacific Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9918992	A1	19990422	WO 1998-IB1720	19981009
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2769505	A1	19990416	FR 1997-12687	19971010
FR 2769505	B1	20000630		
ZA 9809206	A	19990412	ZA 1998-9206	19981008
CA 2312906	AA	19990422	CA 1998-2312906	19981009
AU 9894556	A1	19990503	AU 1998-94556	19981009
AU 762360	B2	20030626		
EP 1027068	A1	20000816	EP 1998-947739	19981009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 504955	A	20021126	NZ 1998-504955	19981009

PRIORITY APPLN. INFO.: FR 1997-12687 A 19971010
WO 1998-IB1720 W 19981009

ED Entered STN: 30 Apr 1999
AB Pharmaceutical compns. for **oromucosal** contact to stimulate host defense mechanisms in a mammal, having an effective amt. of a Th1- or Th2-stimulating cytokine, and methods of treatment with such compns. are

provided.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L115 ANSWER 36 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:745963 CAPLUS
DOCUMENT NUMBER: 128:30389
TITLE: Interferons for stimulation of immune systems
INVENTOR(S): Tovey, Michael Gerard
PATENT ASSIGNEE(S): Pharma Pacific Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9741884	A1	19971113	WO 1997-IB490	19970505
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2253971	AA	19971113	CA 1997-2253971	19970505
AU 9723993	A1	19971126	AU 1997-23993	19970505
AU 724689	B2	20000928		
EP 906119	A1	19990407	EP 1997-919564	19970505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1218408	A	19990602	CN 1997-194501	19970505
BR 9709068	A	20000111	BR 1997-9068	19970505
JP 2000505478	T2	20000509	JP 1997-539696	19970505
NZ 332689	A	20000728	NZ 1997-332689	19970505
TW 482676	B	20020411	TW 1997-86106144	19970507
KR 2000010881	A	20000225	KR 1998-709025	19981109
PRIORITY APPLN. INFO.:			AU 1996-9765 A	19960509
			AU 1996-3959 A	19961203
			AU 1996-4387 A	19961224
			WO 1997-IB490 W	19970505

ED Entered STN: 27 Nov 1997
AB Disclosed are interferon compns. for **oromucosal** contact to stimulate host-defense mechanisms or an immune response in a mammal with a stimulating amt. of the interferon which exceeds parenterally administered amts. of interferon, methods of treatment with such compns. and uses of interferon in the prepn. of such **oromucosal** compns. Mice injected with a LD of encephalomyocarditis virus were successfully treated with 105 IU of interferon-.alpha. by the **oromucosal** route once a day for 4 days.

L115 ANSWER 37 OF 51 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:745962 CAPLUS
DOCUMENT NUMBER: 128:18692
TITLE: Stimulation of host defense mechanisms against **viral** challenges
INVENTOR(S): Tovey, Michael Gerard
PATENT ASSIGNEE(S): Pharma Pacific Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9741883	A1	19971113	WO 1997-IB489	19970505
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2253902	AA	19971113	CA 1997-2253902	19970505
AU 9723992	A1	19971126	AU 1997-23992	19970505
AU 729514	B2	20010201		
CN 1218407	A	19990602	CN 1997-194500	19970505
CN 1218409	A	19990602	CN 1997-194504	19970505
EP 956040	A1	19991117	EP 1997-919563	19970505
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9709066	A	20000104	BR 1997-9066	19970505
JP 2000504026	T2	20000404	JP 1997-539695	19970505
NZ 332690	A	20000728	NZ 1997-332690	19970505
TW 528599	B	20030421	TW 1997-86106145	19970507
ZA 9703987	A	19981109	ZA 1997-3987	19970508
ZA 9703988	A	19981109	ZA 1997-3988	19970508
KR 2000010880	A	20000225	KR 1998-709024	19981109
KR 2000010882	A	20000225	KR 1998-709026	19981109
PRIORITY APPLN. INFO.:			AU 1996-9765 A	19960509
			WO 1997-IB489 W	19970505

ED Entered STN: 27 Nov 1997

AB A method for stimulating host defense mechanisms in a mammal via administering to the mammal a therapeutically effective amt. of an interferon via **oromucosal** contact. The amt. of interferon administered is less than an amt. which induces a pathol. response when administered parenterally. The effect **oromucosal** interferon against viral infection was demonstrated.

L115 ANSWER 38 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2004239136 EMBASE
TITLE: Kinetics of soluble tumour necrosis factor (TNF)-.alpha. receptors and cytokines in the early phase of treatment for chronic **hepatitis C**: Comparison between interferon (IFN)-.alpha. alone, IFN-.alpha. plus amantadine or plus ribavirin.
AUTHOR: Torre F.; Rossol S.; Pelli N.; Basso M.; Delfino A.; Picciotto A.
CORPORATE SOURCE: Dr. A. Picciotto, Department of Internal Medicine, University of Genoa, Viale Benedetto XV, 6, 16132 Genoa, Italy. picciott@unige.it
SOURCE: Clinical and Experimental Immunology, (2004) 136/3 (507-512).
Refs: 33

ISSN: 0009-9104 CODEN: CEXIAL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We have previously studied the effect of three different treatment regimens with interferon (IFN)-.alpha. alone or in combination with amantadine or ribavirin on viral kinetics in the first month of therapy. To understand the regulation of cytokine immune response during early inhibition of HCV replication, we analysed the longitudinal profile of proinflammatory markers (soluble TNFRs), of type 1 cytokines [IFN-.gamma. and interleukin (IL-12)], and of a type 2 cytokine (IL-10). Twenty-two chronic **hepatitis C** patients received daily therapy for 6 months. Sera were collected at baseline, at 6, 12, 24, 30 and 48 h and at the 3rd, 7th, 15th and 30th days of treatment. All cytokines and receptors were evaluated by enzyme linked immunosorbent assay (ELISA). At baseline, a correlation was found between the two soluble TNFRs ($P < 0.0001$) and between the soluble TNFRs and ALT levels ($P < 0.003$), as shown previously. Regardless of the type of treatment, lower levels of soluble TNFR-p75 were present from day 3 in patients who had significant virus decay at day 30 ($P < 0.01$). Baseline IL-10 levels correlated with TNFR-p75 ($P < 0.01$) and with treatment response ($P < 0.05$) and a significant IL-10 reduction from baseline was observed from day 3 among responders, irrespective of the type of treatments ($P < 0.05$). IL-12 and IFN-.gamma.levels did not differ according to treatment or outcome. These findings suggest a pivotal role for IL-10 in orchestrating the antiviral immune response. Its early decline can favour the shift from a Th2 to a Th1 immune response, which has been shown to be associated with a long-term virological response to treatment.

L115 ANSWER 39 OF 51 EMBASE
on STN

ACCESSION NUMBER: 2002155725 EMBASE
TITLE: Developments in the treatment of chronic **hepatitis C**.
AUTHOR: Pockros P.J.
CORPORATE SOURCE: Dr. P.J. Pockros, Div. of Gastroenterology/Hepatology, The Scripps Clinic, 10666 N. Torrey Pines Road, La Jolla, CA 92037, United States. ppockros@scrippsclinic.com
SOURCE: Expert Opinion on Investigational Drugs, (2002) 11/4 (515-528).
Refs: 102
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB **Hepatitis C** virus is the most common chronic, blood-bourne infection, affecting 170 million people worldwide, approximately 3% of the global population. Of those infected with **hepatitis C** virus, 50 - 85% will develop chronic

hepatitis C. Although **hepatitis C** is primarily a disease of the liver, a diagnosis is currently defined by the presence of the **hepatitis C** virus and treatment success is defined by the clearance of the virus. IFN-.alpha. is currently the mainstay of chronic **hepatitis C** therapy; the antiviral and anti-inflammatory components of IFN target both the infectious and the hepatic manifestations of the disease. However, even in combination with ribavirin, interferon therapy is not fully efficacious. Recently, the search for a more effective treatment has led investigators to optimise interferon therapy by developing pegylated interferons. Challenges facing our current treatment of **hepatitis C** virus include lack of efficacy in patients with difficult-to-treat disease, such as patients with cirrhosis or infected with **hepatitis C** virus genotype 1 (who represent a majority of US **hepatitis C** virus infections), the toxicity of combination therapy, the expense and difficulty of therapy and the poor reception of these treatments by many patients. The development of new **hepatitis C** antiviral agents is critical to our management of this disease. A number of approaches are under investigation, including long-acting interferons, immunomodulators, antifibrotics, specific **hepatitis C** virus-derived enzyme inhibitors, drugs that either block **hepatitis C** virus antigen production from RNA or prevent normal processing of **hepatitis C** virus proteins and other molecular approaches to treating **hepatitis C** virus, such as ribozymes and antisense oligonucleotides.

L115 ANSWER 40 OF 51 EMBASE
on STN

ACCESSION NUMBER: 2001360597 EMBASE
TITLE: Combination therapy with interferon-.alpha. and ribavirin for **hepatitis C**: Practical treatment issues.
AUTHOR: Collier J.; Chapman R.
CORPORATE SOURCE: Dr. J. Collier, Department of Gastroenterology, John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9DU, United Kingdom. Jane.collier@orh.nhs.uk
SOURCE: BioDrugs, (2001) 15/4 (225-238).
Refs: 47
ISSN: 1173-8804 CODEN: BIDRF4
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Combination therapy with ribavirin and interferon (IFN)-.alpha. for 6 to 12 months is currently the treatment of choice for chronic **hepatitis C** infection. The overall sustained response rate to treatment, defined as loss of **hepatitis C** virus (HCV) from serum 6 months after completion of treatment, is 40%. The indications for treatment are serum HCV RNA positivity, abnormal serum transaminases and the presence of portal fibrosis and/or moderate/severe inflammation. Response rates are lower in genotype 1 than in genotype 2 or 3 and in the presence of a high viral load. Anaemia is the most common adverse event and is due to ribavirin; neuropsychiatric adverse effects due to IFN.alpha. lead to premature cessation of therapy in 10 to 20% of patients. The current recommended dose of interferon is 3MU given subcutaneously 3 times a week. However, it is likely that longer-acting

pegylated interferons, which may be more effective and can be administered once weekly, will in the future replace currently used IFN.alpha..

L115 ANSWER 41 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000259007 EMBASE
TITLE: Preliminary study of combination therapy with interferon-.alpha. and zinc in chromic **hepatitis C** patients with genotype 1b.
AUTHOR: Nagamine T.; Takagi H.; Takayama H.; Kojima A.; Kakizaki S.; Mori M.; Nakajima K.
CORPORATE SOURCE: T. Nagamine, Department of Health Science, Gunma University School of Medicine, Maebashi, Japan
SOURCE: Biological Trace Element Research, (2000) 75/1-3 (53-63).
Refs: 36
ISSN: 0163-4984 CODEN: BTERDG
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We have evaluated the efficacy of interferon-.alpha. (IFN-.alpha. plus zinc therapy in **hepatitis C** patients with genotype 1b, poor responders for IFN alone. Ten patients were injected with 10 MU of IFN-.alpha. every day for 4 wk, followed by three times a week for 20 wk (control group). Nine patients took 300 mg of zinc sulfate a day orally during IFN-.alpha. therapy (zinc sulfate group), and 15 patients took IFN-.alpha. and 150 mg of polaprezinc (polaprezinc group). On the d 8 of IFN therapy, circadian zinc levels in serum elevated significantly in the polaprezinc group compared to the zinc sulfate group or control group. Serum ALT levels normalized in 73.3% of the polaprezinc group, 55.6% of the zinc sulfate group, and 40.0% of the control group at 6 mo after the end of IFN therapy. Sustained eradication for the **hepatitis C** virus RNA judged at the end of the 6-mo follow-up period was higher in the polaprezinc group than in the zinc sulfate group (53.3% vs 11.1%, $p < 0.05$) or the control group (20.0%). No clinical side effects of zinc were observed at the dose used. The data suggest that polaprezinc is expected to increase the therapeutic response of IFN-.alpha. for chronic **hepatitis C** with genotype 1b.

L115 ANSWER 42 OF 51 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999302857 EMBASE
TITLE: Oral use of interferon.
AUTHOR: Cummins J.M.; Beilharz M.W.; Krakowka S.
CORPORATE SOURCE: Dr. J.M. Cummins, Amarillo Biosciences, Incorporated, 800 West 9th Avenue, Amarillo, TX 79101-3206, United States. JCUMMINS@amarbio.com
SOURCE: Journal of Interferon and Cytokine Research, (1999) 19/8 (853-857).
Refs: 103
ISSN: 1079-9907 CODEN: JICRFJ
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation
031 Arthritis and Rheumatism
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Interferon-.alpha. (IFN-.alpha.) given orally has biological activity in humans and other animals. The dose providing the most benefit delivers IFN-.alpha. to the **oral mucosa** in a concentration (102-103 IU), similar to that naturally produced in the nasal secretions during respiratory infections. In contrast, conventional IFN therapy employs parenteral doses of >106 IU and, for this reason, orally administered IFN therapies have been called low-dose treatments. Efficacy in both animal disease models and human studies has been reported, and the mechanisms whereby oral administration has a systemic effect are under active study in a number of laboratories.

L115 ANSWER 43 OF 51 EMBASE
on STN
ACCESSION NUMBER: 2000021306 EMBASE
TITLE: A multicenter, randomized, controlled trial of three preparations of low-dose oral .alpha.-interferon in **HIV**-infected patients with CD4+ counts between 50 and 350 cells/mm3.
AUTHOR: Alston B.; Ellenberg J.H.; Standiford H.C.; Muth K.; Martinez A.; Greaves W.; Kumi J.; Bykoski J.; Robinson D.; Fitzgerald G.; Pelosi J.; Mallory-Smith M.; Horowitz H.; McCormack W.; Kumar N.; Bubp J.; MacGregor R.R.; Jordan W.C.; Muhammad A.A.; El-Sadr W.; Delapenha R.; Balfour H.H. Jr.; Tangyie G.S.; Friedland G.
CORPORATE SOURCE: B. Alston, Division of AIDS, Natl. Inst. of Allergy/Infect. Dis., 6700 B Rockledge Drive, Bethesda, MD 20892-7624, United States. BA27E@NIH.GOV
SOURCE: Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology, (1 Dec 1999) 22/4 (348-357).
Refs: 18
ISSN: 1077-9450 CODEN: JDSRET
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB To evaluate the effectiveness of low-dose oral .alpha.-interferon (.alpha.-IFN), 247 **HIV**-infected study subjects received placebo, Alferon LDO, Veldona, or Ferimmune in a randomized, double-blind trial. Subjects had CD4+ counts between 50 and 350 cells/mm3 and **HIV** -related symptoms at entry. Study subjects rated the severity of eight symptoms using a symptom burden index (SBI). Study endpoints included changes in SBI, weight, CD4+ count, and Karnofsky score between baseline and the 24-week visit. The SBI outcome and weight were measured in 99 and 106 study subjects, respectively, at both the baseline and 24-week visits. Baseline SBI scores ranged from 5.4 to 7.9 in the four arms. No clinically important or statistically significant differences were found among the four arms with regard to SBI or weight change over the 24-week period. There were also no significant differences among the arms for CD4+ cell count and Karnofsky score. Few adverse reactions were noted in any arm, and there were no significant differences between arms. Although the trial was designed to enroll 560 study subjects and was prematurely terminated because of slow accrual and discontinuations of participants, the small differences among the arms in the primary and secondary endpoints do not support claims of efficacy for the measures studied.

L115 ANSWER 44 OF 51 WPIDS on STN
ACCESSION NUMBER: 2004-108359 [11] WPIDS
DOC. NO. CPI: C2004-044215

TITLE: Method for **oral transmucosal** delivery of interferon involves administering an interferon formulation in the form of an aerosol into a mammal's oral cavity and delivering the interferon by absorption through mucosal tissue.
DERWENT CLASS: B04
INVENTOR(S): POMYTKIN, I A; SVENTYTSKY, E N; TYAGOTIN, Y V; VETELETSKY, P V
PATENT ASSIGNEE(S): (POMY-I) POMYTKIN I A; (SVEN-I) SVENTYTSKY E N; (TYAG-I) TYAGOTIN Y V; (VETE-I) VETELETSKY P V
COUNTRY COUNT: 97
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004000266	A1	20031231	(200411)*	EN	12
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2002330801	A1	20040106	(200447)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004000266	A1	WO 2002-RU300	20020620
AU 2002330801	A1	AU 2002-330801	20020620
		WO 2002-RU300	20020620

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002330801	A1 Based on	WO 2004000266

PRIORITY APPLN. INFO: WO 2002-RU300 20020620
AB WO2004000266 A UPAB: 20040213
NOVELTY - **Oral transmucosal** delivery of interferon, comprising providing an interferon formulation having interferon, administering the interferon formulation in form of solid particles or liquid droplets with mass median aerodynamic diameter of 4-150 micro M sublingually into a mammal's oral cavity, and delivering the interferon by absorption through a mammal's **oral mucosal** tissue, is new.
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - For **oral transmucosal** delivery of interferon (claimed).
ADVANTAGE - The method uses less amount of interferon than the prior art methods; and hence minimizes the potential adverse effects, which may be associated with larger doses of the interferon and still achieves desired therapeutic effects (e.g. **antiviral**, antiproliferative, antitumor, antibacterial and immunoregulatory action of interferon).
Dwg.0/0

L115 ANSWER 45 OF 51 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-706847 [76] WPIDS
DOC. NO. CPI: C2002-200428
TITLE: Composition useful in the treatment of cancer comprises

at least one of incensole or furanogermacrens.
DERWENT CLASS: A96 B05
INVENTOR(S): SHANAHAN-PRENDERGAST, E
PATENT ASSIGNEE(S): (SHAN-I) SHANAHAN-PRENDERGAST E
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002053138	A2	20020711	(200276)*	EN	68
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
EP 1351678	A2	20031015	(200368)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
AU 2002219472	A1	20020716	(200427)		
US 2004092583	A1	20040513	(200432)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002053138	A2	WO 2002-IE1	20020102
EP 1351678	A2	EP 2002-727007	20020102
		WO 2002-IE1	20020102
AU 2002219472	A1	AU 2002-219472	20020102
US 2004092583	A1	WO 2002-IE1	20020102
		US 2004-250535	20040102

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1351678	A2 Based on	WO 2002053138
AU 2002219472	A1 Based on	WO 2002053138

PRIORITY APPLN. INFO: IE 2001-2 20010102

AB WO 200253138 A UPAB: 20021125
NOVELTY - A composition comprises at least one of incensole (I) or furanogermacrens (II), their derivative, metabolite, analog and/or mimic molecule with an additive, a diluent, a carrier, an excipient, or their salts.

DETAILED DESCRIPTION - A composition comprises at least one of incensole (I) or furanogermacrens (II), their derivative, metabolite, analog and/or mimic molecule with an additive, a diluent, a carrier, an excipient, or their salts.

ACTIVITY - Antidiabetic; Cerebroprotective; Antiarthritic; Cytostatic; **Virucide**; Immunosuppressive; Antifungal; Protozoacide; Amebicide; Antibacterial; Vulnerary; Immunomodulator; Antiinflammatory; Neuroprotective; Antiparasitic; Ophthalmological; Keratolytic; Antidiarrheic; Antiasthmatic; Dermatological; Neuroprotective; Hepatotropic.

MECHANISM OF ACTION - Tumor cell growth inhibitor; Endogenous hsp level enhancer; Endogenous precursor dendritic cell level enhancer.

In vitro cytotoxic activity of extracts containing high concentration of incensole and furanogermacren mixture were determined in human melanoma cancer cell line by MTT colonogenic assay. Human tumor (melanoma) cell

lines were grown in RPMI 1640 supplemented with 10 % fetal calf serum and L-glutamine (2 mM). The cells were kept at 5% CO2 and 37 deg. C and passaged routinely, washed and counted. The cologenic assay was performed according to a modified two-layered soft agar assay, where the bottom layer consisted of Iscove's MDM (0.2 ml) with 20% fetal calf serum and 0.75 % agar.

After 24 hours, drugs were added in additional RPMI medium (0.2 ml) with 5-fluorouracil as positive control (100, 300, and 1000 micro g/ml). Cultures were incubated at 5% CO2 and 37 deg. C in a humidified atmosphere for 5-6 days until formation of colonies with diameter of 50 micro m (counts performed with automated image analysis system). Vital colonies were stained with sterile aqueous solution of 2-(4-iodophenyl)-3-(4-nitrophenyl)-5-phenyltetrazolium chloride (1 mg/ml) 24 hours prior to evaluation. The IC50 value for (A) was found to be 0.8 micro m/ml.

USE - This composition is used in the manufacture of medicament for the treatment of a mammal, preferably a neonate, suffering from neoplasia, especially in the sensitization of a resistant neoplasia such as precancerous lesion including syndromes represented by abnormal neoplastic and/or dysplastic, changes of tissue comprising precancerous growths in colonic, breast, renal, central nervous, gastric, or lung tissues, or conditions such as dysplastic nevus syndrome, a precursor to malignant melanoma of the skin, dysplastic nevus syndromes, polyposis syndromes, colonic polyps, precancerous lesions of the cervix (including cervical dysplasia), prostatic dysplasia, bronchial dysplasia, breast, bladder and/or skin and related conditions (actinic keratosis), whether the lesions are clinically identifiable or not, prostate, colon, small and large cell lung cancer, lung adenocarcinoma, epidermoid lung cancer, melanoma (including amelanotic subtypes), renal cell carcinoma, gastric carcinoma, cancers of the central nervous system including brain tumors, neuroblastomas, gastric carcinoma, breast, ovarian, testicular, esophageal, stomach, liver, cervical, adrenal, **oral**, **mucosal**, bladder or pancreatic cancer, lymphoma, Hodgkin's disease, sarcomas, hematopoeitic cell cancers such as B cell leukaemia/lymphomas, myelomas, T-cell or small cell leukemias/lymphomas, null cell, sezary, monacytic, myelomonocytic and hairy cell leukemias; neoplasias in the form of tumor containing epidermoid and myeloid tumor, acute or chronic, nonsmall cell, squamous or solid; immunodysregulatory condition caused by **viral**, extra- or intracellular bacterial, fungal, yeast, extra- or intracellular parasite infection, protozoan parasite, multicellular parasite, autoimmune disease, immunosuppressive therapy, chemotherapy, anti-infective agent therapy, wound, burn, the presence of an immunosuppressive molecule and/or gastrointestinal irritation, due to a DNA or RNA **virus** infection, a parasite infection selected from Trypanosoma (including Trypanosoma cruz, Trypanosoma brucei, Trypanosoma gambiense, Trypanosoma rhodesiense), Plasmodium (Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, Plasmodium ovale, Plasmodium berghei), Cryptosporidium, Entamoeba (including Entamoeba histolytica), Balantidium (including Balantidium coli), Leishmania (including Leishmania brazilienis, Leishmania mexicana, Leishmania donovani, Leishmania tropica), Pneumocystis (including Pneumocystis carinii), Trichomoniasis (including Trichomoniasis vaginalis) or Toxoplasma infection (including Toxoplasma gondii); a Mycoplasma, Listeria or Mycobacterium infection; Streptococcus, Staphylococcus, Vibrio, Salmonella or Shigella infection, enterotoxigenic, enteropathogenic, enteroinvasive or enterohemorrhagic E. coli infection, Yersinia, Campylobacter, Pseudomonas, Borrelia, Legionella or Hemophilus infection; pulmonary Aspergillosis, mucosal or oropharyngealcandidiasis and juvenile paracoccidiomyosis; Candida or Cryptococcus infection; systemic lupus erythematosus, arthritis, asthma, and diabetes; adriamycin treatment, cisplatin treatment, mitomycin C treatment, amphoteracin B treatment; gamma-radiation treatment; nucleoside analog treatment for **viral** infection or for cancer; surgical and accidental wounds,

septic shock caused by surgery; cyclosporin treatment and corticosteroid treatment; irritable bowel treatment, Crohn's disease, wasting syndrome, cachexia, Motor Neuron disease, multiple sclerosis, inflammatory bowel disease, respiratory distress syndrome, chronic diarrhea; cancer; cirrhosis; and/or gram positive multi-drug resistant bacteria. The DNA **virus** infection or the RNA **virus** infection includes retrovirus, togavirus, flavivirus, rubivirus, pestivirus, lipid envelope **virus**, flovirus, picornavirus, **rhinovirus**, coronavirus, respiratory syncytial **virus**, poliovirus, parainfluenza **virus**, influenza **virus**, **hantavirus**, adeno-associated **virus**, measles **virus**, poxvirus, filovirus, human papilloma **virus** and animal papilloma **virus** infection (claimed).

ADVANTAGE - The composition allows the patient to suspend therapy for periods without the worry of inactivity of the drug resulting from the development of resistant cells. The composition exhibits a potent immuno-modulatory effects, provides enhanced antitumor effect and prevents the development of metastasis, overcomes multi drug resistant tumors, and can be administered separately or as a cocktail. The composition regulates immuno responses, and treats neoplasia with minimal toxic side effects unlike the high toxicity associated with standard chemotherapeutic agents. The composition further enhances endogenous hsp levels, and endogenous precursor dendritic cell levels, which results in enhanced immunosurvillence. The composition also upregulates natural killer cells and improves presentation of antigenic peptides to the cytotoxic T cells.
Dwg.0/0

L115 ANSWER 46 OF 51 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-315758 [31] WPIDS
DOC. NO. CPI: C2003-083065
TITLE: Composition, useful for oral or nasal delivery of immunological agents for treatment or prevention of e.g. caries, comprises antigen and signaling molecule.
DERWENT CLASS: B04 D16
INVENTOR(S): SCHOELLHORN, V
PATENT ASSIGNEE(S): (AIDA-N) AID AUTOIMMUN DIAGNOSTIKA GMBH
COUNTRY COUNT: 26
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1260213	A2	20021127	(200331)*	GE	7
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
DE 10125731	A1	20030306	(200331)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1260213	A2	EP 2002-10418	20020508
DE 10125731	A1	DE 2001-10125731	20010517

PRIORITY APPLN. INFO: DE 2001-10125731 20010517
AB EP 1260213 A UPAB: 20030516
NOVELTY - Delivery composition (A) for immunological active ingredients (I), for oral and nasal treatment, especially uptake through the **oral** or nasal **mucosa**, comprises at least one antigen (Ag) and at least one immune signaling material (II), formulated with a carrier.

ACTIVITY - Antibacterial; Antiallergic: **Virucide**;

Hepatotropic; Antiinflammatory; Protozoacide; Cytostatic; Immunostimulant; Immunosuppressive.

No biological data given.

MECHANISM OF ACTION - Vaccine.

No biological data given.

USE - (A) is useful for oral or nasal delivery of immunological agents (claimed) for the treatment or prevention of e.g. caries .(A) are used to stimulate or suppress the immune system, e.g. for prevention or treatment of caries and paradontosis; (food) allergy; **hepatitis C**; mycobacterial infection; malaria and tumors.

ADVANTAGE - By including (II), the dose of Ag can be reduced to 10-50% of that used in conventional subcutaneous or intramuscular injections. Low concentrations of Ag ensure that high affinity T helper cells are induced (rather than a wide range of such cells, some with only low affinity).

Dwg.0/0

L115 ANSWER 47 OF 51 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-483570 [52] WPIDS
DOC. NO. CPI: C2001-145056
TITLE: Predicting responsiveness of a patient to treatment with a **type I interferon** comprising determining the level of induced proteins after treatment with a **type I interferon**,.
DERWENT CLASS: B04 D16
INVENTOR(S): DRON, M; MERITET, J; TOVEY, M G
PATENT ASSIGNEE(S): (PHAR-N) PHARMA PACIFIC PTY LTD; (DRON-I) DRON M; (MERI-I) MERITET J; (TOVE-I) TOVEY M G
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001059155	A2	20010816	(200152)*	EN	133
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001032088	A	20010820	(200175)		
EP 1254263	A2	20021106	(200281)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
US 2003157506	A1	20030821	(200356)		
JP 2003522534	W	20030729	(200358)		148

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001059155	A2	WO 2001-GB578	20010209
AU 2001032088	A	AU 2001-32088	20010209
EP 1254263	A2	EP 2001-904171	20010209
		WO 2001-GB578	20010209
US 2003157506	A1	WO 2001-GB578	20010209
		US 2002-203145	20021126
JP 2003522534	W	JP 2001-558491	20010209
		WO 2001-GB578	20010209

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001032088	A Based on	WO 2001059155
EP 1254263	A2 Based on	WO 2001059155
JP 2003522534	W Based on	WO 2001059155

PRIORITY APPLN. INFO: GB 2000-3768 20000217; GB
2000-3203 20000211; GB
2000-3204 20000211; GB
2000-3205 20000211; GB
2000-3206 20000211; GB
2000-3207 20000211; GB
2000-3208 20000211; GB
2000-3210 20000211; GB
2000-3212 20000211; GB
2000-3213 20000211; GB
2000-3215 20000211; GB
2000-3216 20000211; GB
2000-3219 20000211; GB
2000-3220 20000211; GB
2000-3221 20000211; GB
2000-3222 20000211

AB WO 200159155 A UPAB: 20010914
NOVELTY - Predicting responsiveness of a patient to treatment with a **type I interferon** comprising determining the level of one or more proteins (I) with a 646, 164, 126, 598, 98, 177, 761, 361, 941, 657, 817, 429, 473, 399, 285 or 303 amino acid sequence fully defined in the specification after treatment with a **type I interferon**, is new.

DETAILED DESCRIPTION - Predicting responsiveness of a patient to treatment with a **type I interferon** comprising determining the level of one or more proteins (I) with a 646, 164, 126, 598, 98, 177, 761, 361, 941, 657, 817, 429, 473, 399, 285 or 303 amino acid sequence fully defined in the specification, or their naturally occurring variants or their corresponding mRNAs in a cell sample from the patient obtained following administration of a **type I interferon** or treated prior to determining with a **type I interferon** in vitro.

USE - The method is useful for predicting responsiveness of a patient to treatment with a **type I interferon** (claimed).

ADVANTAGE - Allows a physician to determine whether a patient especially suffering from chronic **viral** hepatitis, neoplastic disease or relapsing remitting multiple sclerosis will respond favorably to **Type I interferon** treatment via **oromucosal** administration decreasing the cost and increasing the benefit of successful treatment.

Dwg.0/0

L115 ANSWER 48 OF 51 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-488749 [53] WPIDS
DOC. NO. CPI: C2001-146711
TITLE: Use of a cytokine antagonist in a pharmaceutical composition to treat autoimmune disease.
DERWENT CLASS: B04
INVENTOR(S): TOVEY, M G
PATENT ASSIGNEE(S): (PHAR-N) PHARMA PACIFIC PTY LTD; (TOVE-I) TOVEY M G
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

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WO 2001054721   A1 20010802 (200153)* EN   23
   RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
       NL OA PT SD SE SL SZ TR TZ UG ZW
    W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
       DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
       LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
       SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001028656   A  20010807 (200174)
EP 1251873      A1 20021030 (200279)  EN
    R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
       RO SE SI TR
US 2003147889   A1 20030807 (200358)
JP 2003531822   W  20031028 (200373)       24
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APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001054721	A1	WO 2001-GB285	20010125
AU 2001028656	A	AU 2001-28656	20010125
EP 1251873	A1	EP 2001-946791	20010125
		WO 2001-GB285	20010125
US 2003147889	A1	WO 2001-GB285	20010125
		US 2002-182062	20021122
JP 2003531822	W	JP 2001-554704	20010125
		WO 2001-GB285	20010125

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001028656	A	Based on	WO 2001054721
EP 1251873	A1	Based on	WO 2001054721
JP 2003531822	W	Based on	WO 2001054721

PRIORITY APPLN. INFO: GB 2000-1710 20000125

AB WO 200154721 A UPAB: 20010919

NOVELTY - Use of a cytokine antagonist which stimulates or enhances T helper 1 cell response for the manufacture of a composition for **oromucosal** administration to inhibit or treat a autoimmune disease, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a pharmaceutical composition which comprises a cytokine antagonist in combination with a carrier or excipient and in a dosage form specifically adapted for **oromucosal** administration.

ACTIVITY - Immunosuppressive; dermatological; antiinflammatory; neuroprotective; antipsoriatic; antirheumatic; antiarthritic; antidiabetic.

No biological data is given.

MECHANISM OF ACTION - T helper 1 cytokine antagonist.

USE - To treat an autoimmune disease preferably associated with abnormal production or activity of IFN- alpha selected from systemic lupus erythematosus, rheumatoid arthritis, type 1 diabetes, multiple sclerosis and psoriasis (claimed).

ADVANTAGE - The anti-**viral** activity of interleukin-2 administered by the **oromucosal** route is reduced by either intravenous or **oromucosal** administration of **Type 1 interferon** antibody.

Dwg.0/3

L115 ANSWER 49 OF 51 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2000-412215 [35] WPIDS
DOC. NO. NON-CPI: N2000-308126
DOC. NO. CPI: C2000-124972
TITLE: Use of **interferon-alpha** for enhancing expression of an aquaporin protein in aquaporin producing cells of a warm-blooded vertebrate having diminished tear production, abnormal mouth dryness and cystic fibrosis.
DERWENT CLASS: B04 C03 P72
INVENTOR(S): CUMMINS, J M; SMITH, K J; SMITH, J K
PATENT ASSIGNEE(S): (AMAR-N) AMARILLO BIOSCIENCES INC; (UYET-N) UNIV EAST TENNESSEE STATE; (CUMM-I) CUMMINS J M; (SMIT-I) SMITH J K
COUNTRY COUNT: 91
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000032387	A1	20000608	(200035)*	EN	24
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW					
AU 2000020318	A	20000619	(200044)		
EP 1147011	A1	20011024	(200171)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE					
US 2002037273	A1	20020328	(200225)		
US 6506377	B2	20030114	(200313)		
AU 763929	B	20030807	(200362)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2000032387	A1		WO 1999-US28045	19991124
AU 2000020318	A		AU 2000-20318	19991124
EP 1147011	A1		EP 1999-963991	19991124
			WO 1999-US28045	19991124
US 2002037273	A1	Provisional	US 1998-109791P	19981125
		Div ex	US 1999-448698	19991124
			US 2001-964792	20010927
US 6506377	B2	Provisional	US 1998-109791P	19981125
		Div ex	US 1999-448698	19991124
			US 2001-964792	20010927
AU 763929	B		AU 2000-20318	19991124

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000020318	A	Based on	WO 2000032387
EP 1147011	A1	Based on	WO 2000032387
AU 763929	B	Previous Publ.	AU 2000020318
		Based on	WO 2000032387

PRIORITY APPLN. INFO: US 1998-109791P 19981125; US 1999-448698 19991124; US 2001-964792 20010927

AB WO 200032387 A UPAB: 20000725
NOVELTY - Enhancing expression of an aquaporin protein (II) in aquaporin producing cells (III) of a warm-blooded vertebrate, comprising contacting the cells with **interferon** (IFN)- **alpha** to upregulate

aquaporin expression in them, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) enhancing saliva production in a patient having a disease causing a dry mouth, comprising administering IFN- alpha in a saliva soluble or miscible form, and holding the IFN- alpha in the mouth to contact the **oral mucosa**, which includes saliva-producing cells;

(2) enhancing lacrimation in a warm-blooded vertebrate having a disease characterized by attenuated function of lacrimating cells, comprising administering IFN- alpha ; and

(3) improving pulmonary function in a patient having a pulmonary disorder characterized by blocked airways, comprising administering IFN-alpha , to upregulate (II) expression in lung cells, and enhance mucous mobilization.

ACTIVITY - Anti-xerotic.

MECHANISM OF ACTION - Up regulation of aquaporin; water homeostasis enhancer. The biological activity of IFN- alpha in increasing aquaporin production for increasing saliva production in was tested in 9 human immunodeficiency **virus** (**HIV**) patients suffering from xerostomia. IFN- alpha was diluted and compressed into lozenges. Three 150 IU lozenges were administered to the subjects 3 times/day and the treatment was continued for a total of 12 weeks. The assessments made were based upon changes in salivary flow rates, oral dryness as reported by the subjects. Changes in unstimulated whole saliva or stimulated whole saliva were studied. 3 of the 9 subjects had a positive response for whole saliva and unstimulated whole saliva. 6 of 8 patients had a clinically significant increase in visual analog scale for oral dryness.

USE - IFN- alpha is used for up regulating aquaporin protein expression in cells exhibiting abnormal dryness is helpful in treating a patient afflicted with the condition causing xerosis, in which the disease condition is alleviated by enhancing the cells ability to release water. Enhanced production of (II) is useful for enhancing saliva production in a patient affected with the disease state producing mouth dryness (xerostomia), for enhancing lacrimation in a warm-blooded vertebrate having a disease state characterized by attenuated function of cells responsible for lacrimation, and for improving pulmonary function in a patient suffering from a pulmonary disorder characterized by mucous blocked airways (claimed). IFN- alpha is also used for treating a patient with cystic fibrosis, or afflicted with abnormal vaginal dryness, and for treating keratoconjunctivitis sicca in dogs.

Dwg.0/3

L115 ANSWER 50 OF 51 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-422868 [36] WPIDS
CROSS REFERENCE: 1996-268530 [27]; 1998-377241 [29]; 2000-061893 [05]; 2000-071668 [05]; 2000-170770 [05]
DOC. NO. CPI: C2000-127890
TITLE: Therapeutic treatment of for example **viral** diseases such as chronic **hepatitis B** and **C**, cancers such as leukemia, and multiple sclerosis comprises administering an immunological tolerance inducing compound prior to an effective drug .
DERWENT CLASS: B04 D16
INVENTOR(S): TOVEY, M G
PATENT ASSIGNEE(S): (PHAR-N) PHARMA PACIFIC PTY LTD
COUNTRY COUNT: 21
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000032223	A2	20000608	(200036)*	EN	26

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU JP US
AU 2000013991 A 20000619 (200044)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000032223	A2	WO 1999-GB4009	19991201
AU 2000013991	A	AU 2000-13991	19991201

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000013991	A	Based on	WO 2000032223

PRIORITY APPLN. INFO: EP 1998-403020 19981202

AB WO 200032223 A UPAB: 20000801
NOVELTY - Therapeutic treatment of a subject with an immunogenic drug comprising:
(a) administering **oromucosally** a first formulation comprising a compound which induces immunological tolerance to the drug; and
(**b**) administering a second formulation comprising the drug that effects the therapeutic treatment.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) A kit for therapeutic treatment of a subject with an immunogenic drug comprising a formulation comprising a compound to induce immunological tolerance to the drug and a formulation comprising the drug to effect the therapeutic treatment;
(2) Using an immunogenic drug for the manufacture of a formulation to effect therapeutic treatment of a disease of a human or animal which has become immunologically tolerant to the drug by the **oromucosal** route of a formulation comprising a compound that induces immunological tolerance; and
(3) Using a compound for the manufacture of a formulation for **oromucosal** administration to a human or animal to induce immunological tolerance to an immunological drug where the human or animal is also administered a second formulation comprising the drug to effect a therapeutic effect.
ACTIVITY - **Virucide**; Cytostatic; Neuroprotective; Immunostimulant; Antianemic; Antibacterial; Immunosuppressive; Antirheumatic; Antiarthritic.
MECHANISM OF ACTION - None given.
USE - For therapeutic treatment of a human or animal. An immunogenic drug or compound is used to manufacture formulations for inducing an immunological tolerance or effecting therapeutic treatment (claimed). **Viral** diseases, such as chronic **hepatitis B** and **C**, **herpes**, and influenza; cancers, such as leukemia, lymphomas and solid tumors; and multiple sclerosis are treated. Neutropenia and leukopenia following chemotherapy are treated. Anemia, chronic renal failure. septic shock and rheumatoid arthritis are treated. Cystic fibrosis and Gaucher disease can be treated by gene therapy.
ADVANTAGE - An immunological tolerance to an immunogenic drug is induced so that when the drug is subsequently administered, its pharmacokinetics and/or clinical effectiveness are improved. Rejection of drugs that are administered in repeat doses over a period of time by the immune system is less likely. The amount of drug that needs to be administered is reduced, lowering costs. Non-humanized antibodies that cannot normally be used for therapy due to rejection by the immune system can be used.

Dwg.0/0

L115 ANSWER 51 OF 51 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1993-288863 [37] WPIDS
CROSS REFERENCE: 1988-147503 [21]
DOC. NO. CPI: C1993-128916
TITLE: Oral, immuno-therapeutic interferon compsn. for treating e.g. multiple sclerosis, rheumatoid arthritis etc. - comprises **interferon** e.g. **alpha** or **beta interferon** and excipient which promotes contact of interferon with **oral** and pharyngeal **mucosa**.
DERWENT CLASS: B04
INVENTOR(S): CUMMINS, J M
PATENT ASSIGNEE(S): (TEXA) UNIV TEXAS A & M SYSTEM
COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 1320905	C	19930803	(199337)*		36
US 5817307	A	19981006	(199847)		
US 5824300	A	19981020	(199849)		
US 5830456	A	19981103	(199851)		
US 5846526	A	19981208	(199905)		
US 5882640	A	19990316	(199918)		
US 6372218	B1	20020416	(200232)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
CA 1320905	C		CA 1987-550816	19871102
US 5817307	A	CIP of	US 1986-927834	19861106
		Cont of	US 1987-110501	19871026
		Cont of	US 1992-875071	19920428
		Cont of	US 1993-9353	19930126
		Div ex	US 1994-305418	19940913
			US 1995-484376	19950607
US 5824300	A	CIP of	US 1986-927834	19861106
		Cont of	US 1987-110501	19871026
		Cont of	US 1992-875071	19920428
		Cont of	US 1993-9353	19930126
		Div ex	US 1994-305418	19940913
			US 1995-479958	19950607
US 5830456	A	CIP of	US 1986-927834	19861106
		Cont of	US 1987-110501	19871026
		Cont of	US 1992-875071	19920428
		Cont of	US 1993-9853	19930126
			US 1994-305418	19940913
US 5846526	A	CIP of	US 1986-927834	19861106
		Cont of	US 1987-110501	19871026
		Cont of	US 1992-875071	19920428
		Cont of	US 1993-9353	19930126
		Div ex	US 1994-305418	19940913
			US 1995-476621	19950607
US 5882640	A	CIP of	US 1986-927834	19861106
		Cont of	US 1987-110501	19871026
		Cont of	US 1992-875071	19920428
		Cont of	US 1993-9353	19930126
		Div ex	US 1994-305418	19940913
			US 1995-475753	19950607

US 6372218	B1	CIP of	US 1986-927834	19861106
		Div ex	US 1987-110501	19871026
		Cont of	US 1991-775291	19911009
		Cont of	US 1993-3624	19930113
			US 1995-381136	19950131

PRIORITY APPLN. INFO: US 1987-110501 19871026; US
1986-927834 19861106; US
1992-875071 19920428; US
1993-9353 19930126; US
1994-305418 19940913; US
1995-484376 19950607; US
1995-479958 19950607; US
1993-9853 19930126; US
1995-476621 19950607; US
1995-475753 19950607; US
1991-775291 19911009; US
1993-3624 19930113; US
1995-381136 19950131

AB CA 1320905 C UPAB: 20020521
An oval dosage form of interferon for nunan use comprises 0.01-5 IU of interferon per pound of body wt. and excipients selected to promote contact of interferon with the **oral** and pharyngeal **mucosa** of the patient.

Also claimed are (i) an immuno-therapeutic dosage formulation in the form of an effervescent tablet, which releases 0.01-5 IU of interferon per lb. of body wt. on effervescent dissolution in water and (ii) an immuno-therapeutic dosage form comprising 0.01-5 IU of interferon/lb. of body wt. and excipient allowing contact of interferon with the **oral** and pharyngeal **mucosa** of patient, which is held in the mouth.

USE/ADVANTAGE - Compsn. is used to potentiate disease-corrective immune responses in warm-blooded animals afflicted with immunoresistant diseases, characterised by hyper- or hypo-active immune system function. Compsns. are used to effect remission of neoplastic disease, hyperallergenicity, immuno-resistant or -debilitating **viral** infections and autoimmune disorders showing chronic tissue degenerative inflammation, e.g., multiple sclerosis, rheumatoid arthritis, stomatitis, lupus erythematosus, compsn. alone or in combination can be used to effect remission of cancers, e.g., malignant lymphoma, melanoma, mesotheliane, Burkitt lymphoma and nasopharyngeal carcinoma and other neoplastic diseases. Human **viral** infections which compsns. can be used to treat are human **rhinovirus** (common cold), **herpes** simplex I **virus** (cold sores) and human papov (warts). Admin. is by dosages of 0.01-5 IU/lb. body wt./per day. Daily dosage is singularly or in a multiple-dose daily regimen. A staggered treatment of 1-3 days/week or month can be used as an alternative to continuous daily treatment.
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